

Outsmarting The Number One Killer

A Science-based Program for Reversing Atherosclerotic Plaque, Heart Attacks and Strokes

by

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Notice

This book is intended as a reference volume only, not as a medical manual. The information given here is designed to help you make informed decisions about your health. It is not intended as a substitute for any treatment that may have been prescribed by your doctor. If you suspect that you have a medical problem, we urge you to seek competent medical help.

Outsmarting The Number One Killer

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Plaque, Heart Attacks and Strokes**

by

Timothy J. Smith, M.D.

“About three quarters of the population of the USA older than 30 years has some lesion related to atherosclerosis in the arterial tree. This lesion gets worse almost every day in all these people and will eventually result in closure of a vital artery in half of them, causing their death.”

William P. Castelli, M.D. Director, Framingham Heart Study

Part One: The Disease

Chapter 1

A Journey of the Heart

Dad's Heart Attack

It was 2:45 AM. I was sixteen years old and asleep in my bed. In the distance someone moaned "I can't breathe!" Just a bad dream, I thought, and drifted back to sleep. But there it was again...

"I can't get my breath!"

Suddenly wide awake, I recognized my father's voice coming from down the hall. There was a kind of urgency in it that I'd never heard before.

I jumped up and dashed to my parents' bedroom. Dad sat on the edge of the bed, slumped forward, breathing hard, clutching his chest—his face pale, almost bluish. Mom was biting her lower lip the way she always did when she was real worried.

"What's wrong?" I asked.

"It feels like there's an elephant standing on my chest," Dad groaned.

"What do you think it is, Harry?" asked Mom.

"I don't know. Maybe a little indigestion—something I ate for dinner," replied my father. "Just 'a piece of underdone potato'..."

My father's endearing way of dealing with scary stuff was to make light of it, and there he was, at it again, trying to calm us with a joke/quote from Dickens' *A Christmas Carol*. Cute—but I wasn't buying it. I figured my parents might fritter away valuable time debating the possibilities, so I picked up the phone and dialed our family physician, Dr. Hess, who—amazingly—answered on the second ring. He asked a few quick questions, then told me, "Tim, your dad's having a heart attack. You need to get him to the hospital right away. Do you have a car?"

"Y-yes." I stammered.

"Get him over to the ER as fast as you can. I'll meet you there."

"Oh, okay. Thanks," I stammered. "Sorry to bother you in the middle of the night..." As I struggled to express my appreciation he interrupted me with five words that changed my life. "*That's what your doctor's for*. Now get your dad to the ER."

We jumped in the car and fifteen minutes later an EKG at the hospital showed Dad was indeed suffering a myocardial infarction.

In the middle of an emergency, you don't have time to think about what you do and why you do it—you just do what needs to be done. Later on, though, I had a couple of realizations. The first was that Dr. Hess—with those unforgettable words—had shown me that he cared, that he had a *heart*. "*That's what your doctor's for*." Wow! This guy, roused from sleep, had every reason to be grumpy, but instead he sincerely viewed the situation as an opportunity to help. I remember thinking that if I ever became a doctor, that was the kind of doctor I wanted to be. When I'm called in the middle of the night, or a particularly demanding patient is hassling me, or when my work load seems overwhelming and I just want to get away, Dr. Hess' words—and even the sound of his voice—pop back into my head, reminding me how important it is for a doctor to *care*.

The spirit of "*That's what your doctor's for*" extends to this book. I have been blessed with a multifaceted career that has guided me toward a unique understanding of how to prevent and reverse our "Number One Killer," atherosclerotic heart and cardiovascular disease—and if that information someday saves your life or that of a loved one, perhaps I will have lived up to the standard set by Dr. Hess on that frightening night half a century ago.

Another realization came years later. When Dad was in the midst of his heart attack, it never occurred to me that he might actually die. His chances of croaking on the spot, were, in fact, about fifty-fifty—and if he had, my life would have been so very different in so many ways that it's frightening to think about it. My father was such a strong, supportive figure that without him I would not have had the moral (not to mention the financial) support I needed to complete medical school. If Dad's heart attack had killed him, I wouldn't be sitting here writing a book about how to prevent death from a heart attack.

Here's another irony: In the fifty years since that night, atherosclerotic plaque—I'm tempted to call it atherosclerotic *plague*—remains just as deadly as it was then. This is true despite the

awesome achievements of modern medicine. Research into cell and molecular biology has shown us the exact mechanisms by which atherosclerosis kills. We have also learned about natural medicines that address—and reverse—the specific biochemical causes of the disease. Unfortunately, this valuable information is not yet applied in clinical practice. We're still chugging along in the Model T of drugs and surgery while a molecular biological Maserati gathers dust in the garage.

Shadowing Dr. Swank

My senior year in medical school was capped of with a required six-month rotation in surgery. For one of those months, my classmates and I “shadowed” a surgeon. Each of us was assigned to a different university staff surgeon whom we followed religiously, day and night. If our surgeon was called in the middle of the night, we got up too. If our surgeon was summoned to the ER, we went too. This exercise in immersion allowed us to see and do everything typically done in a busy surgical practice.

It was my great good fortune to have been assigned to cardiovascular surgeon *par excellence* Humphrey Swank, M.D., generally acknowledged as the local hotshot. Revered by all—especially us wannabe docs—Swank had been immediate past president of the county medical society, and had won numerous other awards and accolades. His reputation as a surgeon's surgeon was deserved. The chance to study with him represented a great learning opportunity and my classmates were green with envy. (“You got assigned to Swank? Whoa!”)

Looking back from a more mature perspective, I wonder now why anybody would relish the opportunity to get up at 4:30 AM for rounds, scrub in for surgery at 6:00, then stand in one place for many long hours viewing one grisly surgical scene after another—witnessing some patients come back to life and others die. But I did relish it. At the time the blur of pacemaker insertions, cardiopulmonary bypasses, carotid endarterectomies, valve repairs and replacements, and aortic aneurysm repairs all seemed pretty exciting.

I'll never forget my first day with Swank. He had a gentlemanly warmhearted air about him that helped me realize immediately why everyone—profs, hospital staff, patients, and students—loved him. He welcomed me with a strong handshake and a big friendly smile. His first words to me were, “I trust your experience with me this month will be gratifying.” The way he said it suggested more expectation than hope, as if it were my job to make sure my experience was rewarding. “You're going to see a lot of interesting stuff in the next month,” he continued. “You'll be scrubbing in with me for every surgery. We'll see all the in-hospital patients on rounds together and you'll sit with me in my office for all the outpatient appointments. Can you hold retractors? Suture? Stand in one place for eight hours without a break if necessary? Endure repetitive questions from anxious patients?”

“Yes, *sir*.” I answered, with all the exuberance of a medical student in the presence of a surgical god.

“Well, then, Dr. Smith, let's scrub in.”

Surgeons tend toward brashness—sometimes to a fault—but Swank never slid across that thin line that separates self-confidence from arrogance.

Later that morning, having completed a couple of pacemaker insertions and a valve repair, on our way to a late lunch, Swank told me, “Tim, I've been at this for 35 years now, and the heart

continues to amaze me. Other organs multitask but the heart serves just one purpose: that of pushing blood through the body. It contracts and relaxes about 100,000 times every day. You have already studied the precise pathways blood follows as it flows through the various chambers and vessels. In your lifetime, your heart will pump about a million barrels of blood. If blood were oil, that would be enough to fill three supertankers.”

Between morning surgery and afternoon rounds, Dr. Swank insisted on hosting me for lunch at the exclusive City Club. Hoping I’d choose a career in surgery and maybe even follow in his prestigious footsteps, he wanted to familiarize me with some of the extra perks of the hot shot surgeon experience. Every weekday for my month with Swank, we had a fabulous lunch (especially when compared with the humble soup or sandwich my frugal student’s budget would have otherwise allowed). I sipped away at my Calistoga water while he knocked back a couple of martinis and told wonderful tales, all true—ranging from his surgical feats to unvarnished tidbits about his personal life—which was clearly in shambles. A nasty divorce. Greedy lawyers. A disappointing teenage son. The thrill was gone...except for the surgery. I started wondering whether the stress of his life made it all that special. Then, entering another world, we’d hop back into his snazzy red 1969 Oldsmobile Toronado convertible, cruise back to the medical school, and zip through rounds—popping in on the same patients we’d had our hands inside of that morning, or a day or two before. We’d visit three or four different local hospitals and see a couple dozen cases before calling it quits. Two days each week we’d do initial interviews and outpatient follow-up in his splendid 15th floor office, featuring an entire wall packed with degrees, diplomas, and honors showcasing his accomplishments.

My month with Swank had been exciting and intellectually stimulating, but as it drew to a close, something gnawed at me. It wasn’t the gory scenes; in medicine one gets used to blood and guts. It wasn’t the hideous hours; getting up early and working long hours was standard fare. Nor was it the guy’s personal problems; all too often that comes with the territory. Finally I figured it out: woven into the fabric of Dr. Swank’s wonderful work—all those high-tech repair jobs—was a backdrop of futility. Specifically, it occurred to me, nobody was getting cured. Sure, Swank provided some extra mileage for worn out hearts, but none of his skills addressed the underlying atherosclerotic disease process that had caused his patients’ problems in the first place. I wanted—I needed—to figure out how to close the barn door *before* the horses had bolted. I figured there must be a way to *prevent* these heart attacks and strokes. At the time I had no way of knowing it would take a few decades—and over 40 million more deaths—before molecular biology would finally solve the riddle of atherosclerosis.

Zebras and Chickens

My first clue about the overwhelming seriousness of the atherosclerosis problem came in my third year of medical school.

Any doctor can tell you that physicians-in-training—and their professors—exhibit a strong tendency to get excited about the “zebras”—the rare, unusual, and thought-provoking diseases—while ignoring the boring everyday “chickens.” Backaches, PMS, and the common cold are chickens. Thrombotic thrombocytopenic purpura and Charcot-Marie-Tooth disease are zebras. While we may have learned more by focusing on the zebras, we really needed to learn about the

chickens too, because those would be the ones we would see and treat most often. Atherosclerosis turns out to be one humongous chicken.

My freshman and sophomore years in medical school had been all about the necessary but borrrrring basic sciences: anatomy, physiology, biochemistry, pathology, pharmacology, microbiology, etc. When we weren't studying books, we spent our time sitting in lecture halls, peering intently into our microscopes at microbes and tissue samples, or dissecting our cadaver. The only contact with real, live patients was when an occasional "case" was wheeled into the lecture hall or surgical amphitheater and presented to all 100 of us simultaneously. Junior year the fun began. We got to dress up in whites and hit the wards and clinics, acting like real doctors, interviewing and examining real live patients with real diseases rather than the ones we studied on pathology slides and pickled organs. We were pumped about that.

The first week of junior year found me in a hospital ward conference room with about fifteen classmates, bantering as we waited for our professor to show up. At a lull in the conversation, I wondered out loud what might be the most common disease, the "Number One Killer"? It seemed that we should be giving that one—whatever it was—more attention than the zebras that seemed to be on everyone's mind. (Okay, maybe I was swimming upstream here, but it wouldn't have been the first time—nor would it be the last.) Surprisingly, no one knew. Our intern showed up, so we asked her, but she didn't know either. I went home and pored over my fat medical textbooks (there was no Google box back then) until I found the answer: atherosclerosis. Hmmm. We *had* been seeing a lot of heart attacks, strokes, and peripheral vascular disease.

Now, forty-plus years later—with an impressive array of medical discoveries behind us and even more ahead—guess what's *still* the most common disease?

Back then the plaques and heart attacks and strokes caused by atherosclerosis seemed to appear magically out of nowhere. We hadn't a clue about the etiology (the underlying causative mechanisms) of atherosclerosis. Now we do. Over the years since I was a medical student, researchers in cell biology and molecular medicine have painstakingly unraveled this incredibly complex puzzle. Thousands of pieces have fallen into place, and medical science has finally achieved a thorough understanding of the complex sequence of events that culminates in a heart attack or a stroke. We now understand why arteries harden, how plaque forms, and what causes the blood clots that block arteries and kill or disable people by the millions. Researchers have identified the key biochemicals that cause atherosclerosis and it is now possible—even easy—to test for these markers to determine your atherosclerosis risk.

As our molecular biological understanding of atherosclerosis has matured, parallel research in nutritional biochemistry has revealed a diverse array of natural agents that block and reverse the causes of atherosclerosis. All are molecules normally present in the body, and, as such, they are experienced as "friendly." These food-derived medicines—herbs, enzymes, hormones, vitamins, minerals, essential fatty acids, amino acids, food extracts, and phytopharmaceuticals (plant-derived medicines)—"belong" in your body and your body instantaneously knows it. Those "friendly" natural medicinal substances are managed by your biochemical systems as if they were—and indeed, in most cases they actually are—real food. We call this "biocompatibility." Drug medicines are not biocompatible and predictably elicit toxic reactions. Pharmaceutical medicines trigger cellular reactions designed to "detoxify"—in other words, "kick out the culprit." This is why drugs almost invariably have side effects, toxic reactions, and other signs of incompatibility. Natural nutritional medicines don't do that.

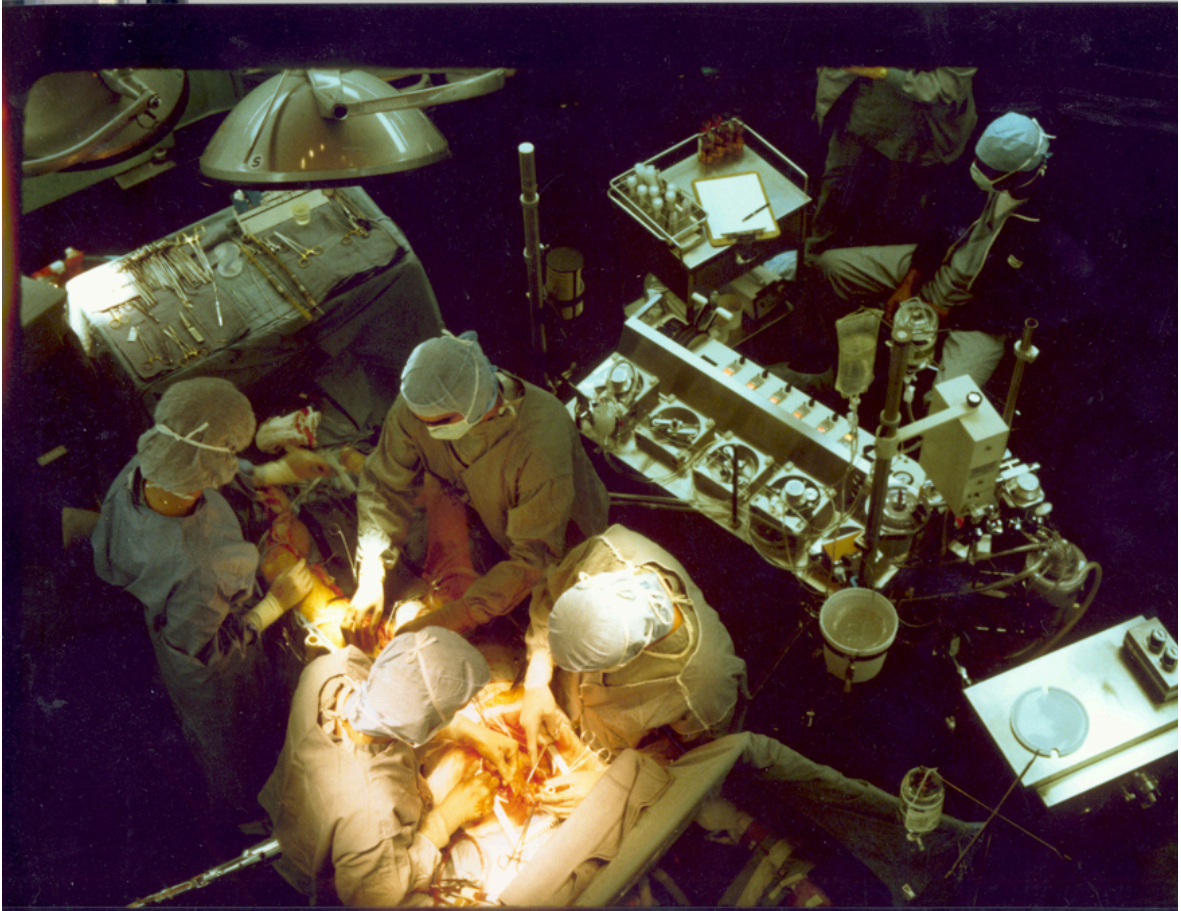
Beyond biocompatibility, there's another huge reason natural medicines are preferable to drugs. While pharmaceuticals exert their effects by suppressing symptoms, natural medicines actually support and nourish the healing process.

Let me give you a few quick examples of natural medicines that prevent and reverse heart disease. *Pomegranate juice* reverses atherosclerosis. *Methylfolate* (a B-complex vitamin) prevents the homocysteine accumulation that irritates and damages blood vessels. *Red yeast rice extract*, a Chinese Traditional herbal medicine, lowers cholesterol and C-reactive protein gently and naturally. *Curcumin*, the active ingredient in the spice turmeric, reverses inflammation and discourages excess blood clotting. *Nattokinase*, an enzyme derived from soy, gently dissolves the clots that block blood vessels. *Green tea extract*, a powerful antioxidant, lowers cholesterol and prevents endothelial damage. *Serrapeptase*, another enzyme, dissolves atherosclerotic plaque and blood clots. I could go on and on—and I will, later in this book.

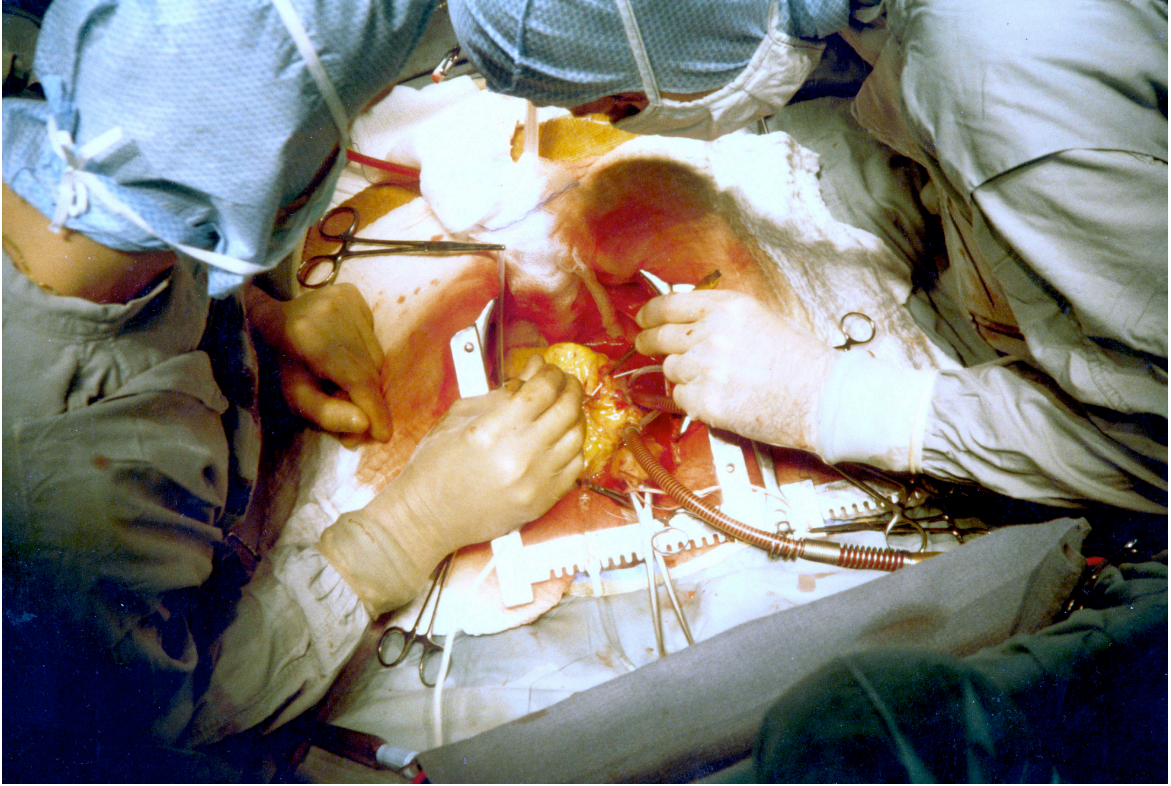
Unfortunately, there's a huge disconnect between these research findings and their clinical application. Doctors simply don't know about this stuff. Even though simple nutritional medicines like pomegranate juice, green tea, and turmeric have been shown beyond any doubt to address and reverse the molecular biological causes of atherosclerosis, physicians continue to prescribe a complex array of symptom-suppressing drugs and surgical techniques—Band-Aids that don't cure anything.

Why is the average doctor oblivious to these powerful healing agents? One must wonder whether the profit motive plays a role. After all, food-based medicines are unpatentable and therefore unprofitable. The dark political and economic forces that drive our dysfunctional health care delivery system work hard to suppress the free flow of information about natural medicines. But, really, those forces are beyond the scope of this book. Suffice it to say that we need a system where drug and insurance companies are not running the show. I believe most of us would welcome a shift away from the profit motive and back toward patient *care*—the kind exemplified for me when I was 16 by Dr. Hess.

Don't hold your breath. There are few signs of imminent change. While we wait, we need to be proactive, which—in terms of The “Number One Killer”—means [get tested](#), and, if your markers are abnormal, follow the recommendations in this book. *Atherosclerosis can be prevented, and even advanced disease can be reversed. It is exceedingly unlikely that your doctor knows this yet.* Can you—can any of us—afford to wait until he or she figures it out?



Coronary artery bypass surgery depicting vein harvesting from the legs (left of image), establishment of bypass (bottom of image), and perfusionist beside heart-lung machine (upper right). Patient's head (not seen) is at the bottom.



Open chest closeup.

Bypass Surgery

I often think about my poker buddy Dwight, who, in 1981, was diagnosed with severe stenotic arteriosclerotic coronary artery disease. Dwight's left anterior descending artery had become completely obstructed by plaque. Bypass surgery—nicknamed CABG for Coronary Artery Bypass Graft (pronounced “cabbage”)—was his only option. Dwight's surgeon, Dr. Stanley Morgan, invited me to scrub in.

Two days later I found myself gowned, gloved, and backing through the OR door, hands held high. In the center of the room on the surgical table lay Dwight, bare-chested under bright lights, prepped and thoroughly anesthetized. He was fully anesthetized and unconscious. At his side stood Dr. Morgan, going down his pre-op checklist. He glanced up and gave me a quick, “Hi, Tim,” then went back to his preparations.

I was greeted cheerfully by Dr. Ben Jones, the perfusionist, whose job was to keep Dwight's blood circulating while the surgeon worked on his heart.

“What kind of music do you like?” he asked.

“That's an odd question,” I thought. Sensing my confusion, he pointed at the controls of a high tech stereo system built-into his command console. The cardiopulmonary bypass machine featured a state-of-the-art sound system complete with compact cassette.

“These procedures can take four, six, even eight hours, and good music helps us pass the time.”

“Oh. Well, I like *both* kinds,” I quipped, “country *and* western.” He gave me a funny look, so I quickly added, “...but I’m eclectic. Anything’s okay.” (Hip-hop and rap hadn’t yet been invented or I might have had to make some exceptions.) “How about classical?”

Dr. Morgan made sure everyone was ready, then put his scalpel to Dwight’s chest and swiftly made a long, deep vertical midline incision that exposed the breast bone. “Sternal saw, please.”

The acrid, nauseatingly familiar odor of instantaneously vaporized flesh washed over us as Morgan sliced deeper and deeper into Dwight’s chest. In a few minutes Dwight’s pericardial sac was exposed to the bright surgical lights. Dr. Morgan gently slit it open with his scalpel, exposing Dwight’s beating heart.

It’s hard to do surgery on a moving object. To stop the heart from beating, Dr. Morgan injected 500 cc of potassium chloride into the aortic root. Two more beats and Dwight’s heart stopped cold. I looked up at the EKG monitor and noticed the flat line.

Dr. Morgan now quickly hooked up the heart-lung machine that would cool, oxygenate and pump Dwight’s blood until the obstructed coronary artery could be removed and the bypass graft stitched into place.

It’s more than a little creepy to gaze into a friend’s open chest and view his exposed heart. That had stopped beating. Technically, my friend Dwight was dead.

As Dr. Morgan accessed Dwight’s heart, a second surgeon, Dr. Hale, had been carefully dissecting (we call it “harvesting”) his saphenous (leg) vein, the piece of living tubing that would replace the blocked anterior descending coronary artery. Dr. Hale now gingerly handed the piece of vein to Dr. Morgan who then meticulously stitched it into place.

Dwight’s heart was then restarted. The big concern at this stage was a leak in the stitching when blood pressure returns to the heart, and we breathed a collective sigh of relief when Dwight’s sutures all held.

Dr. Morgan wired Dwight’s sternum back together and sutured the skin back in place over it. Four hours of intense concentration, but now he was done. He pulled off his gloves and took a deep slow breath.

Bypass surgery has come a long way since Dwight’s procedure. The new cardiology sports a high-tech and amazing array of options including endoscopy, angioplasty, valve replacements, stents, and creative new imaging techniques. I have nothing but awe and respect for the incredible skills and dedication of cardiologists, cardiovascular surgeons, anesthesiologists, and perfusionists—a hardworking and committed breed of doctor. They save thousands of lives. Yet nothing would make me happier than to put them out of business. Research shows this can be done. It’s time to apply what we know and make the leap from high-tech barn door closing to prevention and reversal. This book will explain how.

As the astonishing life and death drama of Dwight’s bypass operation unfolded before my eyes, I couldn’t help but wonder how things had gotten so bad for him (and millions like him) that all this technology and surgical skill had become necessary. I remember thinking there must be a way to head this off at the pass. But what was it? Another quarter century would pass before researchers would fully unearth the molecular biological causes of atherosclerotic coronary artery disease, but now we do have a definitive picture. The disease is now curable. Parallel developments in nutritional biochemistry have provided dietary information and an armamentarium of natural nontoxic medicines that address—and reverse—the causes of the disease.

Late afternoon the next day I returned to the hospital and rode the elevator up to the Intensive Care Unit to see Dwight. He was still a little groggy from the anesthesia, so I just stood there next to his bed, gazing at the monitors and thinking about yesterday. After a while he realized I was there.

“Hi, Tim,” he mumbled.

“Hi Dwight. How are you doing?” I asked.

“Still in a fog, Tim—but, strangely, I’ve got more energy. I feel better.”

This didn’t surprise me. Due to the clogged vessels, Dwight’s heart muscle cells had been suffering prolonged starvation. Now, thankfully, they were getting the nutrients and oxygen they needed.

“It must have been strange to be actually looking at my heart. That doesn’t happen very often.”

“Yeah,” I answered, “as experiences go, I just can’t pigeonhole that one.”

“I guess they got it fixed up and running again, or we wouldn’t be here chatting.”

A lump swelled up in my throat. A short “Yup” was all I could manage.

Suddenly a stocky, white-gowned woman with a blank expression entered carrying a tray of food which she unceremoniously plunked down onto Dwight’s bedside table. She skedaddled without a glance, a smile, or a word.

Dwight’s first post-surgical meal! A little cloud of steam lifted off as he raised the cover. We both glanced at it, then at each other. First we frowned, then broke out in laughter. *Oh my god!* The irony was so thick you could cut it with a scalpel (or perhaps a butter knife). On the tray—and I am not making this up—sat a small, well-marbled overcooked steak with plenty of extra fat around the edge, perhaps harvested from a plaque-laden candidate for a bovine bypass in some parallel universe. Alongside the meat, four or five anemic canned string beans peered up at us. The “salad” consisted of a single leaf of lettuce on which sat a chunk of artificially colored (it had that “day-glo” look) green Jello, internally sprinkled with a few small pieces of canned pear. Beside the plate was a single slice of white bread and a pat of butter. Dessert was a little square piece of white cake topped with a buttery sugary frosting. The (by then well-established) connection between diet and heart disease had somehow eluded the nutritionist who assembled this culinary debacle that shouted up at us, “Want another heart attack? Just eat me.”

As our scientific understanding of atherosclerosis has flowered, so, too, has our appreciation of the potent effects of various foodstuffs on arterial health. Even back in the early eighties when Dwight’s surgery was done, we knew that certain foods (e.g., animal fat, white flour, refined foods, sugars, processed food, chemical additives, sugar, and saturated fat) encouraged atherosclerosis. As you’ll see later in this book, subsequent research has revealed that many foods discourage and even reverse atherosclerosis. If an enlightened nutritionist had fashioned Dwight’s post-surgical meal applying what we know today, it might have contained nuts, beans, and small portions of very lean meat—perhaps a stir fry or curry spiced with turmeric (which contains curcumin). Broccoli or artichoke or just about any vegetable. A salad with garlic, onion, leafy greens, tomato, carrot, and a dressing made with flaxseed oil and vinegar. Dessert might be fresh fruit. A glass of pomegranate juice or a cup of green green tea. There’s an almost infinite number of possibilities of heart-protective foods to choose from—and you’ll see lists of them in later chapters.

Mr. Fan Has a Heart Attack

“Hey, Tim, wanna catch a Raider’s game with me this weekend? It’s free.”

My buddy Donny—a fellow physician—was on the line.

“Free?” I asked.

“They need docs in the stands in case a fan needs medical attention. I’ve done it a couple of times already, Tim, and nobody’s gotten sick so far. We’ll probably just watch the game and then go home.”

Seemed like a good deal to me, so—oblivious to how complicated my life was about to become—I said, “Sure.”

Fast forward to a sunny Sunday afternoon at the Oakland Coliseum. It was 1978 and the Oakland Raiders were about to take on the Seattle Seahawks. After the head doctor briefed us, we lugged our emergency supply bag up to our free 50-yard line seats and relaxed—ready to go to work if necessary, but not expecting any excitement beyond what the game would generate. Early in the second quarter an usher shouted to us from the aisle. “Hey! Doc! Someone’s real sick—right over *there!*” He pointed about twenty rows over, where we easily spotted the gentleman I will call “Mr. Raiders Fan” (we never did learn his real name), sprawled on the cement walkway beside his seat.

We grabbed our medical gear and dashed over. We got to him in just a few seconds but he was already unconscious and unresponsive. No pulse. No respiration. No diagnostic challenge here: Mr. Raiders Fan was having a heart attack. We immediately initiated CPR. Donny did the chest/heart compression while I tried in vain to insert the plastic airway. Mr. Fan’s vomiting reflex frustrated my attempts to get a breathing tube in. As luck would have it, right at that moment a guy emerged from the crowd and huddled down next to us over the patient with some very welcome news.

“I’m an anesthesiologist and I can get that airway in for you.”

“Great,” I replied and quickly handed it to him. I moved aside and watched him successfully insert it on the first try. What a relief! Now Mr. Fan was able to get plenty of air.

At that point we felt we had a good chance of saving him.

The next day’s *Oakland Tribune* featured a photo. The bottom half showed me, Donny, and the mystery anesthesiologist—backs to the camera—squatting over Mr. Fan’s lifeless body. Above and behind us, facing the camera, were platoons of fans, standing up so they could see *over* us. Not a single person was looking down at us! None of them showed the slightest interest in the struggle to save a fellow human’s life. I wonder if they’d have paid closer attention if they’d known their own odds of having a heart attack were roughly one in two—and the odds they’d survive that attack were about the same.

After we had worked on Mr. Fan for a few more minutes, two paramedics arrived. Together we hefted Mr. Fan up onto a gurney and rolled him through the crowd and out to their ambulance, then sped off—sirens blaring—to Oakland’s Highland Hospital, where, despite the best ER code blue technology...well, the outcome was not good. Let’s just say this was Mr. Fan’s last hot dog, last beer, and last football game—and he would have been disappointed that the Raiders lost the game to the Seahawks—by a single point.

Dancing with death

Mr. Fan had been dancing with death for quite a while. At the time, we couldn't explain why Mr. Fan had a heart attack, but now, 30 years later, with the wisdom of hindsight, it is safe to say that atherosclerotic vascular disease had been eroding his arteries—from the inside out—for decades. Assuming his case was typical, fatty yellow patches of atherosclerotic plaque covered much of his abdominal aorta by the time he was ten years of age. Now in his late forties, plaque had invaded the walls of many of his blood vessels, including those of his coronary arteries.

Most of the plaque deposited over the years in the walls Mr. Fan's vessels would have healed and hardened in place, and thus posed no immediate threat to his health. A small section of his anterior descending coronary artery (the main branch that supplies the left front of the heart), however, contained "unstable plaque," a fragile, incompletely healed scab-like affair that can easily break, causing local bleeding and clot formation. During the second quarter of the Seahawks game this unstable plaque burst like a broken pipeline, spewing out its contents. A large clot (or thrombus) quickly formed at the site of the rupture. This clot stopped the hemorrhage, but in the process created a bigger problem; it became a roadblock that prevented passage of crucial nutrients and oxygen to the heart muscle downstream. Within seconds, Mr. Fan's heart stopped beating.

Mr. Fan's condition was far from unique. Just about everybody in the western world has some degree of atherosclerosis. According to William P. Castelli, M.D., director of the renowned Framingham Heart Study, "About three quarters of the population of the USA older than 30 years has some lesion related to atherosclerosis in the arterial tree. This lesion gets worse almost every day in all these people and will eventually result in closure of a vital artery in half of them, causing their death." Mr. Fan was on the short list.

In 1978 we didn't know what caused atherosclerosis, and we didn't know why some atherosclerotic vessels broke and bled, while others didn't. Donny and I did know, however, that a blood clot had developed inside a major vessel in Mr. Fan's heart and was blocking blood flow through it. It would take researchers another quarter century to figure out exactly what triggers the formation of these cataclysmic clots.

Endothelial damage and dysfunction causes atherosclerotic plaque, heart attacks, and strokes

Now, with the wisdom of hindsight, it is safe to say that Mr. Fan's problems began and ended in his *endothelium*, the single layer of cells that lines the inside of all blood vessels. Discovered in 1973, the endothelium was originally thought to be passive and inert, and that oxygen, carbon dioxide and nutrients passively diffused through it. Nothing could be further from the truth. We have learned that the endothelium is a strategically-positioned, proactive *organ* that makes vital metabolic decisions and exerts powerful control over the farthest reaches of our bodies. The total length of your circulatory system is about 100,000 miles, every single one of which is lined with a continuous sheet of endothelial cells. Placed side-by-side, the endothelial cells from a single human would wrap more than four times around the circumference of the Earth. The total endothelial surface area is 4000-7000 square meters, which, if spread out flat, would cover roughly the same area as a football field.

The endothelium is a highly selective semi-permeable membrane that maintains internal order by deciding what stays in the bloodstream and what gets past it into the wall of the blood vessel (and then beyond to every organ and tissue in the body). The endothelium monitors and

manages the transit of thousands of blood-borne entities—from the smallest molecules to large proteins to (relatively) huge white blood cells—into and out of the bloodstream. Though immune health and inflammation management—two key features of cardiovascular health—head up the list of functions that depend on endothelial health, one would be hard-pressed to find a bodily function *not* directly influenced by it. When damaged, the endothelium fails—and when it fails, bad things happen. Like Mr. Fan’s heart attack.

Prolonged endothelial exposure to irritants causes atherosclerotic plaque, a kind of scar tissue that forms in the walls of vessels that are trying to heal from ongoing injury. Protecting your endothelium from damage is the first and most important step in outsmarting the “Number One Killer.” The [heart marker blood tests](#) discussed in this book will detect the presence of endothelial damage—and even tell you what’s causing it. This information, available for less than \$200, is empowering because it tells you what is going to cause *your* heart attack or stroke. Then, by applying the information provided in this book, you can reverse it.

You’d think that an organ as large and important as the endothelium would be taken seriously by mainstream medical clinicians, but it’s not. Endothelial damage, dysfunction, and failure causes the myocardial infarctions and strokes that account for the vast majority of mortality in the western world, but you’d have a hard time finding a doctor who could tell you what the endothelium is, much less what it does or why it’s important. Finding a doctor—even a cardiologist—who could tell you how to fix a broken endothelium would be even more difficult. That kind of information is an important piece of “what your doctor is *for*”—so I will tell you, in this book, how to determine whether your endothelium is damaged, what damaged it, why that translates directly into cardiovascular disease risk, and how to make it healthy again.

Some causes of endothelial dysfunction

- High blood pressure (hypertension)
- Diets high in animal fat
- Diets high in carbohydrates and sugars
- Diets low in fruit and vegetables
- Elevated blood levels of glucose, fibrinogen, C-reactive protein, homocysteine, and/or cholesterol
- Depletion of antioxidant nutrients
- Pesticides and herbicides in non-organic food
- Fast food, junk food, processed food
- Air and water pollutants
- Chlorination (e.g., city tap water)
- Heavy metals (e.g., mercury in fish)
- Environmental chemicals (e.g., pesticides on food)
- Alcohol
- Smoke

Solving the riddle of atherosclerosis

Nutrition—what you *do* eat and what you *don’t* eat—plays a powerful role in causing, preventing, and even reversing atherosclerotic vascular disease. A lifestyle laced with stuff on the above list will generate plaque. Avoiding these items will protect you against endothelial damage and atherosclerosis.

Most Americans have already developed advanced atherosclerotic heart disease. How can you determine whether you are among them? The disease is “silent,” so you won’t have symptoms or signs (like chest pain or shortness of breath) to alert you. This is where state-of-the-art biochemical medicine comes in handy. Lab testing—specifically a fasting blood sugar, C-reactive protein, homocysteine, fibrinogen, and a lipid panel—will tell you whether endothelial dysfunction and plaque are busily at work eroding your arterial health. And if they are, diet and natural medicines can and will reverse it. I’ll provide a lot more detail about this in later chapters, but I want to start by telling you how I would have treated Mr. Fan if he had come into my office a month or two before the Seahawks game (assuming we knew then what we know now).

After a thorough history and physical examination, I would have ordered the above-listed tests. Then, while waiting for the test results, I would have prescribed four remarkable nutritional medicines, each of which will reverse atherosclerosis *regardless of cause*: pomegranate juice, curcumin, nattokinase, and serrapeptase.

(Most doctors, when confronted with coronary artery disease, are so heavily programmed to prescribe drugs like statins, beta blockers, and anticoagulants that they are unaware of the huge array of powerful nontoxic nutritional medicines that accomplish something no drug can do: *reverse* atherosclerosis. This is not a casual statement; it is supported by thousands of peer-reviewed scientific studies published in the scientific literature. See [References](#).)

Mr. Fan’s pomegranate juice must be pure, unadulterated, and organic. This delicious sweet ruby red juice melts away atherosclerotic plaque and encourages damaged endothelial membranes to heal. It lowers cholesterol by blocking synthesis in the liver, lowers blood pressure (risk factor for heart attacks), and exerts a gentle natural anticoagulant effect that reduces the risk of vessel-blocking blood clots (kind of like baby aspirin but without being an irritating foreign chemical). If that weren’t enough, pomegranate juice is the most powerful fruit-derived antioxidant, and has been shown to reduce oxidative stress everywhere in the body. This incredibly versatile food also blocks osteoporosis, beefs up immune function, and provides potent protection against breast, prostate, and colon cancer. And it tastes great!

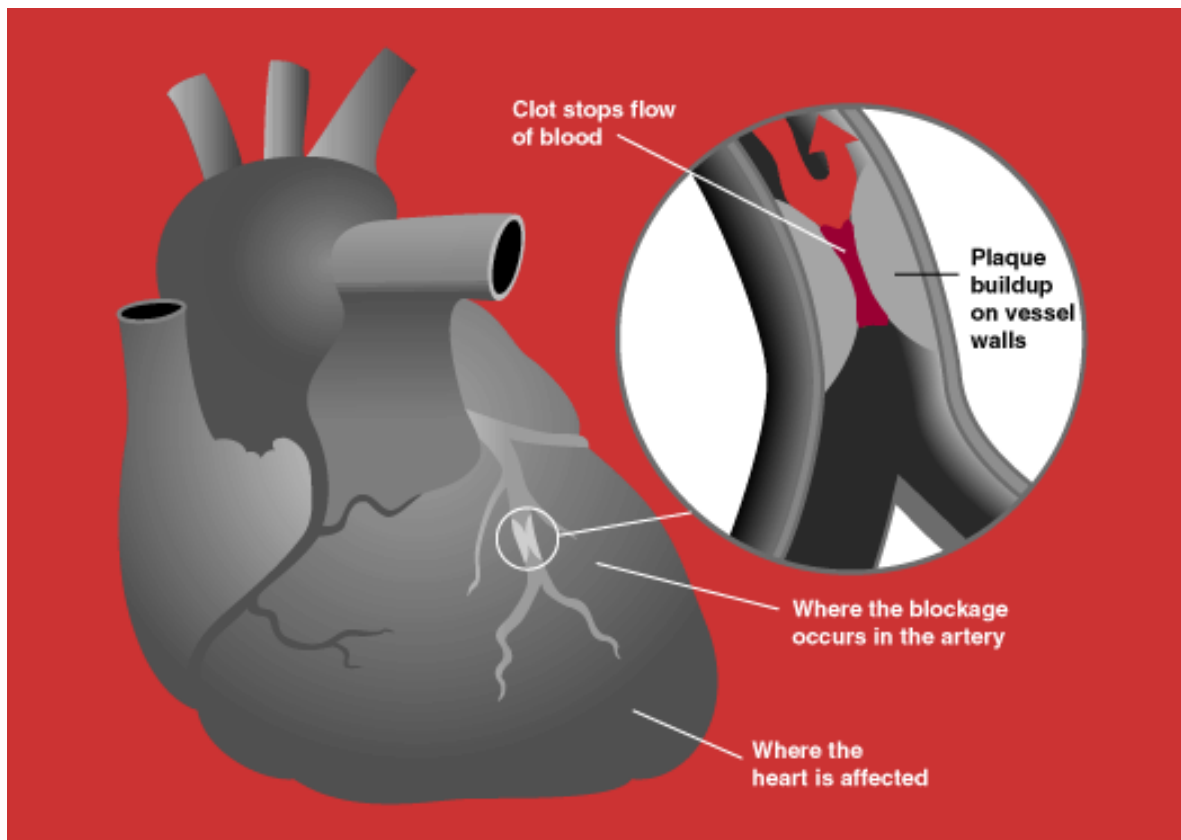
The anti-inflammatory herb curcumin (the active ingredient in the curry spice, turmeric) blocks initiation and progression of atherosclerotic plaque. Best provided in combination products containing supportive anti-inflammatory herbs such as rosemary, holy basil, green tea, ginger, coptis, barberry, skullcap and Protokin, curcumin lowers cholesterol, LDL, fibrinogen, and C-reactive protein; it reverses endothelial damage, protects LDL from being oxidized, and prevents blood clots like the one that killed Mr. Fan. Because curcumin is poorly absorbed, stick with turmeric “phytosome” products in which the curcumin has been bonded to a carrier molecule, usually phosphatidylcholine.

The third nutritional heart medicine I’d recommend is serrapeptase (Serralase), an anti-inflammatory enzyme that reverses atherosclerosis by dissolving away the fibrin scaffold upon which plaque is deposited. Serrapeptase also digests and removes thrombi, those artery-blocking blood clots (again, constructed from the fibrin generated by fibrinogen). Originally discovered centuries ago by Chinese Traditional Medicine herbalists, serrapeptase is the enzyme secreted by the silkworm moth to digest its way out of its cocoon. The modern version is cultured from bacteria, purified, and made into a tablet.

After I got Mr. Fan started on a program of nutritional medicines to reverse his heart disease, we’d have some long chats about dietary choices. I’d recommend fresh whole foods and

a low carb (minimal grains and no sugars) diet. Though small portions of lean meat are acceptable, the main focus needs to be on vegetables, fruit, beans, nuts, and seeds.

In the short run, yes, it might be easier to use drugs to suppress Mr. Fan's symptoms, but I'd rather put the principals of molecular biology to work removing the *causes* of his heart disease. Our understanding of the fundamental science behind atherosclerotic plaque—coupled with an appreciation of the biochemistry of nutrition—now make that possible. Mr. Fan was born a quarter century too soon.



A myocardial infarction occurs when atherosclerotic plaque builds up slowly in the inner lining of a coronary artery and then suddenly ruptures, causing catastrophic thrombus (clot) formation, totally occluding the artery, and preventing blood flow downstream.

Chapter 2

Atherosclerosis: The Silent Killer

Atherosclerosis will be the cause of *your* death, more likely than not, unless you take action to find and treat its causes. No matter who you are, how successful or wealthy you are, no matter what your age or sex or where you live, your chances of dying prematurely of cardiovascular disease are about three in four.

Atherosclerosis (from athero = artery and sclero = hardening) is the buildup of plaque in the walls of our arteries. Plaque may eventually block the flow of blood, causing a heart attack or a stroke. Atherosclerotic cardiovascular disease, by far the leading cause of death for both men and women in the United States, begins in childhood and develops silently for decades.

At this moment, more than 70 million Americans suffer from some form of atherosclerotic cardiovascular disease. Most of the rest are in the process of developing it.

Twice every minute, an American suffers a heart attack. Half of these heart attacks—about one every minute—is fatal. Two-thirds of these victims had no warning, no early symptoms to tell them they might be at risk; the first and only symptom was sudden death. That's why it's known as "the silent killer."

Our current (dysfunctional) approach to vascular disease

The current standard medical approach for "preventing" atherosclerotic cardiovascular disease (ASCVD) is to correct your cholesterol if it's elevated (usually with statin drugs) and lower your blood pressure if it's up (more drugs). If you're lucky, your physician might take an extra 30 seconds and toss in some gratuitous recommendations about exercise and a low-fat diet. The next step is usually to kick back and wait for a cardiovascular "event." No problem: more often than not there'll be one. Nothing like a medical emergency to mobilize action. Now the doctors whip out their prescription pads and sharpen their scalpels in a belated attempt to "close that barn door."

First a prescription for some overpriced cardiovascular drugs. There's a vast array—all big moneymakers for the pharmaceutical industry (which has spent mightily on ads that encourage doctors to write those prescriptions). If the drugs don't work, or if the atherosclerotic arterial blockage has progressed too far, there's always angioplasty, a surgical procedure in which a small balloon is inserted into the narrowed part of the blocked vessel and then inflated to stretch it open. At this time, a "stent" may also be implanted. A stent is an expandable wire mesh tube that is placed inside the artery to keep it open. The arterial blockage often progresses, and bypass surgery may be required. Here, a leg vein is transplanted to the heart to get blood past the blockage. By now you may be wondering how things got this far out of control. The long-term survival statistics on stents, angioplasties and coronary bypasses are disappointing because none of these fancy medical maneuvers addresses the actual *causes* of the problem. So it keeps coming back.

A shift of consciousness is required

It seems to me that there's something deeply flawed about a health care delivery system that twiddles its thumbs, waiting patiently while Rome burns, then screams, "Fire!" after all the damage is done.

If our health care system offered an effective program for prevention, none of these heroic measures would have been necessary. When driving, you don't wait until the last second and then try to swerve away to avoid a crash. You take preventive action from the earliest moment when a potential danger becomes apparent. That's the kind of shift in consciousness I'm advocating for our medical approach to heart disease. From a statistical standpoint we know that most of us are steering toward a cardiovascular 'event' of some kind. Let's inform ourselves and start taking preventive action now,

Medical scientists now know that atherosclerotic cardiovascular disease is both *preventable* and *reversible*. By taking the blood tests I describe in this book, you can see the train wreck coming long before it actually happens. And you'll know which markers are going to cause it.

By identifying and reversing your specific risk markers, you can dramatically reduce that 75% risk down to 5% or less. You can remove the causes of the "Number One Killer" before they remove you.

Rethinking atherosclerosis, the "Number One Killer"

As a nation, we have been sold on the notion that to prevent heart disease all we have to do is control our cholesterol, weight, and blood pressure, quit smoking, and eat a low-fat diet. Like Hal, Celeste, Art, Jake, and Chip in the next chapter, you may be convinced that you are doing everything in your power to minimize personal risk. It may surprise you to discover that your risk of a potentially fatal heart attack or stroke—despite your low cholesterol—could still be very high. In this book I'll explain how to apply important recent research findings showing how to identify and sidestep the causes of the heart attacks and strokes that kill most of us.

When a heart attack or a stroke occurs, powerful molecular biological forces have been silently at work for decades, gradually setting the stage for the devastating event. Our understanding of atherosclerosis has now advanced far beyond the simplistic and antiquated notion that cholesterol is at the root of it. Using molecular medicine we can now identify the imbalances leading to heart attack and stroke, and then alter the biochemical landscape to put the body back on track. Early detection allows us to use diet and gentle natural medicines rather than harsh drugs.

If you already suffer from atherosclerotic heart and cardiovascular disease, I'll show you how to identify and repair abnormal markers so your blood vessels can heal. Even if you are perfectly healthy and symptom-free, you can use the heart markers to literally see into your future; you can identify the factors that damage blood vessels and reverse them to prevent a health disaster.

Chapter 3

Hal, Celeste, Art, Jake and Chip

Five Case Studies

Hal

Hal felt great at 50. This was no accident. For his entire adult life he had worked hard to stay healthy: he exercised an hour a day, kept his cholesterol under control, didn't drink or smoke, maintained a healthy weight and blood pressure, managed his stress, rarely ate meat or dairy, avoided fast and processed foods, and got regular checkups.

One might then wonder why Hal had a heart attack while cutting grass in his backyard one sunny Saturday afternoon. He clutched at his chest, gasped, then collapsed. His wife, Muriel, delivering some lemonade and cookies, found him slumped unconscious on the ground next to his power mower.

Fortunately, Muriel was a nurse. She immediately began CPR, and after several minutes of chest-pounding and mouth-to-mouth resuscitation, managed to revive Hal just as the paramedics showed up.

Hal had been very close to death, but he was one of the lucky ones. For about a third of all heart attack victims, the first symptom is sudden death.

While hospitalized, Hal discovered my heart disease program. He got tested, and learned to his dismay that his C-reactive protein level had been "off the chart" at 8.3. We started him on the diet, nutritional supplements, and exercise program that would eventually reverse his atherosclerosis. Today Hal is happy and healthy again. His C-reactive protein is normal, his coronary arteries are plaque-free, and he's back to mowing his lawn.

Celeste

Celeste, a 55-year-old Chicago real estate broker, was an avid reader of health magazines and knew a lot about how to stay healthy. Thanks to a statin drug, her cholesterol was normal. She had a tendency toward high blood pressure, but kept it under control by exercising every day and eating a vegetarian diet. She wouldn't dream of smoking.

One afternoon, on her way home from the office, Celeste passed out at the wheel and crashed into an elm tree. She had suffered a massive stroke. Celeste survived, however, and was referred to my clinic by a good friend. Biomarker testing told us that Celeste's unmeasured and untreated Fibrinogen level had been quite elevated at 384 (normal is less than 250).

Fibrinogen is a pro-inflammatory protein that causes clots to form in arteries. Celeste's left middle cerebral artery had become suddenly and completely blocked, cutting off the blood supply to a large segment of her brain. Had her fibrinogen remained elevated, she would have almost certainly suffered another stroke.

Celeste and I developed a reversal program of diet, exercise, and natural medicines; she has adhered to it and her brain has healed. She is back at work selling lots of great real estate. Every year for the past ten years she has sent me a bouquet of roses and a touching note that says, "Thank you Dr. Smith for saving my life."

Art

At sixty-two, Art felt healthy and vital. A musician and avid skier, Art took great pride in the fact that his cholesterol was always under 200. He exercised every day, eschewed fatty foods, and didn't smoke. He kept his stress level and blood pressure low by playing piano and living a laid-back lifestyle. At a recent checkup, his internist told him he had no sign of heart or cardiovascular disease and that his general health was "perfect." A couple of weeks later, one wintry afternoon, Art slumped over his keyboard while practicing with his band. Fortunately, the bass player dialed 911, and with instructions over the phone kept Art alive until the paramedics got there.

Art's heart attack was not due to an elevated cholesterol level; it was caused by undiagnosed and untreated "metabolic syndrome" (also known as insulin resistance or Syndrome X), an extremely common condition in which elevated fasting blood sugar accelerates the atherosclerotic hardening of arteries. Art's fasting blood sugar was far above normal at 121. His triglycerides were also high at 350, and his protective HDL-cholesterol was depressed at 30 (should be above 45).

Jake

Jake was in the prime of his life. A forty-something businessman from San Francisco, he headed up his own advertising firm, where he played tough and called all the shots. At home, however, Millie, his wife and sweetheart of 25 years, was the real boss. She understood his soft side and exploited it by teasing him mercilessly. He loved to play with his kids and reveled in watching them grow up.

Jake took good care of his health—at least he thought he did. His father and grandmother had died of heart attacks, so Jake knew he needed to be extra careful. To his dismay, Jake's cholesterol had been creeping up in recent years. His internist, Dr. Bob Sweeney, had given him a statin drug to bring it down, and when Jake's cholesterol reached the normal range, Sweeney had pronounced him "healthy as a horse" and "free of heart attack risk."

About two weeks after his last visit to Dr. Sweeney, while roughhousing with Mikey, his seven-year-old son, Jake stopped suddenly and clutched his chest. He turned blue and collapsed on the Oriental rug. In less than five minutes, Jake was dead.

A routine homocysteine level check could have saved his life. Homocysteine is an irritating amino acid our bodies generate in the normal course of metabolism. Certain B-complex vitamin deficiencies can block the proper removal of excess homocysteine, causing a buildup that escalates risk for heart attack, stroke, and a raft of other diseases. My staff located the sample of blood that had been used to test Jake's cholesterol, and we ran a homocysteine test on it. Jake's homocysteine had been extremely high at 14.7 (ideal is 6.2 or less).

The point I am making here is that paying attention to the new heart markers could save your life. Conversely, it could be costly to stay stuck in the fantasy land of "Fix your cholesterol with a statin and you're home free."

Chip

Now let's take a look at a more *hopeful* case, that of Chip, a 48-year-old dentist who came to see me five years ago because he had read my book, *Renewal: The Anti-Aging Revolution*, and wanted to work with me on an anti-aging program.

Before starting him on a program I examined his “biochemical landscape” to spot any life-shortening abnormalities. In other words, I ordered my usual battery of blood tests. Chip’s lipid panel and cholesterol were normal, but all five remaining heart disease markers (homocysteine, C-reactive protein, fasting blood sugar, fibrinogen, LDL particle size) were elevated, effectively putting him on a collision course with a heart attack. We discussed this in his follow-up visit:

“Chip, your test results here tell me there are major problems in your cardiovascular system. You are at very high risk of a heart attack or stroke.”

“I don’t understand, doc. My internist told me my heart was fine. My blood pressure, cholesterol, and LDL have never been elevated, I don’t smoke, I eat almost no animal fat, I’m not overweight, and I have never had any symptoms that would suggest a problem with my heart.”

“Chip, nowadays, we have far better tools than cholesterol and LDL for predicting atherosclerotic heart and cardiovascular disease. Your ‘independent markers’ for heart disease are telling me your risk is high.”

“What are these ‘independent markers’?”

“As a medical professional you may have heard of some of them. They are fasting blood sugar, C-reactive protein, homocysteine, fibrinogen, and LDL particle size.”

“And mine are all elevated?”

“Yes, some more than others, but all are high.”

“What do these ‘new markers’ actually tell you, doc?”

“Good question. They are the molecular ‘bad guys’ that cause atherosclerosis. We have a thorough understanding of the mechanisms that lead up to heart attacks and strokes, far superior to what we had 50 years ago when the cholesterol connection was discovered. The molecular biology of the arterial hardening and heart attack processes is very well understood by researchers in the field. These new markers are literally the molecular bad guys that cause atherosclerosis. We can measure them, and when any of them is present, your risk is high.”

“Does this mean I am doomed to have a heart attack?”

“No, but it does mean that, based on the research behind these markers, unless we get them back to normal, your risk is very high.”

“What do we need to do?”

“I am going to put you on a program of diet, exercise, and nutritional supplements. This will gradually bring all your markers back to normal, and with them, your risk will go from very high to very low.”

“Doc, not to question your insight into these things, but you are asking me to trust some numbers on a piece of paper. How do I know I am preventing anything if I don’t already have symptoms or signs of heart disease?”

“Well, Chip, you put your finger on the problem. Let me try to explain. You do have choices. You can wait until you have a heart attack, and then—assuming you survive—address the problem. Or you can familiarize yourself, as I have done, with the huge body of research evidence that tells us these markers provide an extremely accurate assessment of risk. And it’s reassuring—to those of us who consider ourselves good scientists—that these markers are not just innocent bystanders to the atherosclerotic process. They are the key players, the molecular villains that cause the problem. So when we see them, there is no question that trouble is ahead, and when we make them go away, we can be sure that we have averted a disaster. This molecular biological approach epitomizes our new direction in modern medicine. Now we can use nutritional medicine to head off disorders that accelerate aging and shorten lifespan.”

“That is why I am here, Dr. Smith.”

Chip diligently followed the program I laid out for him. Gradually (it took over a year), he got all his markers back into the normal range. Though he never had a symptom (there’s a reason we call atherosclerosis the “silent killer”), Chip appreciates the fact that we averted a heart attack, and may just have saved his life.

Though millions die every year of preventable heart attacks and strokes, you do have a choice. Like Chip, I want to show you how to outsmart the “Number One Killer.”

Atherosclerosis

- **Causes more deaths *every year* than all the wars in history combined**
- **Kills two out of every three persons, more than all other diseases combined**
- **Preventable and reversible**

Chapter 4

An Epidemic of Staggering Proportions

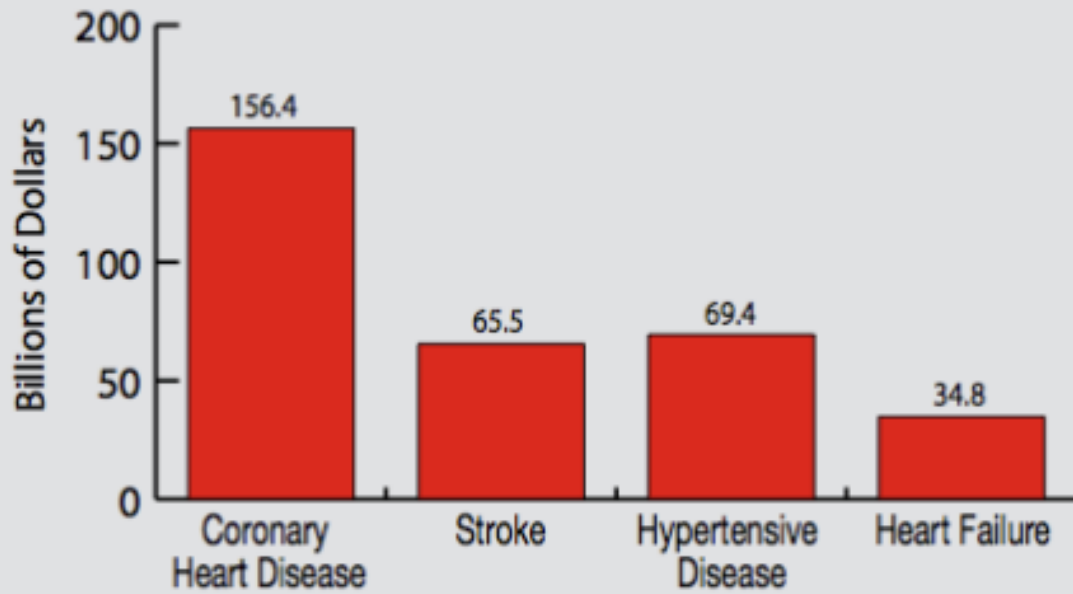
This is an epidemic

Like ostriches with our heads in the sand, we are living in the midst of a modern epidemic, oblivious to the fact that most of us will succumb to it.

Coronary artery disease is—by far—the biggest killer of all. Stroke is number three. No other modern illness comes close to reaping as grim a toll on human life as atherosclerotic cardiovascular disease. The term “epidemic” fails to capture the enormity of this public health problem. Consider these staggering statistics:

- Heart disease is by far the number one cause of death for both men and women in the United States.
- The death rate from atherosclerotic cardiovascular diseases is *three times as high as all other causes of death combined*.
- Your personal odds of dying from atherosclerotic cardiovascular disease are overwhelming: it kills three of every four people.
- Americans suffer 1,500,000 heart attacks a year—that’s one every 30 seconds.
- In the U.S. alone, these heart attacks claim over *one million lives every year*—that’s 3000 deaths every day.
- *Every 60 seconds*, someone in the United States suffers a fatal heart attack.
- For one out of every three first-time heart attack victims, that heart attack was their last.
- Heart disease is a serious problem for women. Heart disease kills more women over the age of 60 than any other disease. At 500,000 lives a year, it dwarfs breast cancer, which claims about 50,000 annually.
- The death risk goes up with age: 84% of persons aged 65 or older die of this disease.
- Over one-fifth of the entire U.S. population—over 57 million Americans—suffers from some diagnosed form of cardiovascular disease, and most of the rest will get it.
- Cardiovascular disease is the leadingcrippler as well: 10 million Americans are disabled by cardiovascular conditions every year.
- Surgeons continue to perform close to half a million bypass operations a year.
- Worldwide, cardiovascular disease accounts for about 50% of all deaths.

**Estimated Direct and Indirect Costs (in Billions of Dollars) of Major Cardiovascular Diseases and Stroke
United States: 2008**



Source: NHLBI.

Our outmoded system

Whether measured in terms of human suffering or dollars, the cost of this epidemic is outrageous—and unnecessary.

“Gargantuan” would be a reasonable term to describe the economic impact of cardiovascular disease on the U.S. health care system. The Centers for Disease Control (CDC) estimates that the cost of heart disease and stroke in the United States exceeded \$500 billion in 2010. By way of comparison, the total annual budget, at around 2 trillion, is only four times as much. To quote the late Senator Everett Dirksen of Illinois, “A billion here, a billion there, and pretty soon we’re talking real money.”

Coronary artery disease has spawned a multibillion dollar industry that features advanced techniques that generate huge profits for the “medical-industrial complex.” Bypass surgery, balloon angioplasty, cardiac catheterization, stents (a wire meshed affair that is inserted inside a blocked artery to keep it open), and prescriptions for an array of expensive, symptom-suppressive, high-tech drugs. It isn’t as if these methodologies don’t work; they do—at least in the short run. But none of the sophisticated tools described above addresses the actual *causes* of vascular disease, so it progresses regardless. Bypass surgery and its ilk are useful only *after* the disease has become life threatening. Why not enable prevention by putting more of those big bucks into addressing the *causes* of the disease?

The irresistible profitability of modern cardiovascular medicine creates a huge problem. Prevention—though relatively inexpensive and easily attainable—isn’t capable of generating the kinds of insane revenue streams as drugs and surgery. Prevention, in fact, erodes profits by removing future customers. It starves the beast and therefore threatens the very existence of the extremely lucrative coronary artery disease industry.

A new approach

This human tragedy can now be averted by detecting the earliest stages in the development of heart disease. This can be accomplished long before symptoms appear. When abnormal test results reveal dark clouds on a patient’s cardiovascular horizon, we now possess the technology to reverse the risk. Modern cell biology has delivered a detailed understanding of the evolution of the atherosclerotic disease process (see *Atherogenesis*, Chapter 5). We can “see” the biochemical fingerprints of atherosclerosis long before overt symptoms appear. Using the heart markers described in this book, we can sort through the complexities of cell biological function, identify the disruptive forces, and then fix them before they cause a disaster.

At this point in the evolution of our understanding of cardiovascular disease, only a handful of physicians apply the revolutionary molecular medical discoveries of the past ten years that allow us to identify and prevent or reverse atherosclerosis. Most doctors continue to adhere to the tragically archaic notion that all they need to do is lower cholesterol and blood pressure (with the appropriate drugs, of course—a statin here, a calcium channel blocker there), suggest a low-fat diet and some exercise, and *voilà!*—“prevention.”

The cardiovascular industrial medical complex and its 25-billion-dollar statin industry wants to keep the doctors—and you—thinking that all you’ll ever need are drugs and surgery. We need to question the “experts” who insist on waiting until heart disease has reached an advanced state, and then roll out the very profitable hardware of medical desperation. Millions of lives would be

saved by altering our approach. Researchers have identified and extensively characterized the molecular “risk markers” that are *causally* related to heart attack and stroke. Though it may take the health care delivery system decades to shift over to early identification, you can implement these discoveries on a personal basis right now. Get the tests listed below. If any of your markers are abnormal, you know you are at risk, and by studying the chapter that discusses that marker you will know exactly why you are at risk. I’ll explain what you need to do to repair the malfunctioning biochemical system so that the marker—and your heart disease risk—returns to normal. Retesting will tell you whether your program is working.

Doctors need to understand that the key to preventing heart attacks and strokes is early detection (in other words, testing for the six heart markers described below). Abnormal markers need to be treated with gentle natural medicines. Reversing the abnormal markers will halt the progression of the disease process, and go on to reverse it. Detecting atherosclerosis in its early, reversible stages allows the use of gentler, plant-based medicines that support the body’s healing systems. This obviates the necessity of using toxic drug medications that mask the symptoms.

The six heart markers

The six heart markers I recommend for identifying the underlying causes of heart attacks and strokes are:

- **The Lipid Panel**—the basic lipid panel includes: **cholesterol, triglycerides, LDL, HDL, and VLDL**. See Chapter 7.
- **C-Reactive Protein (CRP)**—CRP is a marker for inflammation that causes coronary arterial damage. See Chapter 8.
- **Homocysteine**—an amino acid that is harmless at normal levels, but, when elevated, inflicts caustic damage to the walls of your blood vessels. See Chapter 9.
- **Fibrinogen** (fibrinogen *activity*, not fibrinogen antibody)—a pro-inflammatory protein that, when elevated, damages arteries, causing atherosclerosis. Fibrinogen also plays a major role in the formation of the blood clots (thrombi) which can block cerebral and coronary arteries. See Chapter 10.
- **Fasting Glucose**—a fasting blood sugar level provides information about how well the body is regulating blood sugar. High fasting levels are indicative of dysfunctional blood sugar regulation or “insulin resistance.” Chronically elevated blood glucose damages arterial walls and dramatically accelerates atherosclerosis. See Chapter 11.
- **LDL particle size (“VAP”)**—the size of your LDL particles is a powerful determinant of cardiovascular risk. Smaller LDL particles (we’re talking a few nanometers—a few billionths of a meter—here) are big troublemakers, because they can easily slip through the inner arterial lining (the endothelium) and cause atherosclerotic damage. Larger particle size is strongly correlated with decreased risk. See Chapter 12.

An elevation of any one of these markers spells trouble. Taken together, these tests constitute an exceptionally accurate set of tools for predicting cardiovascular risk, for identifying this disease before it happens—and for reversing it before it maims or kills.

Everyone is different. You might have elevated cholesterol and fibrinogen, while your friend might have elevated homocysteine, C-reactive protein, and fasting blood glucose. Any combination of markers is possible, so, when it comes to treatment programs, there can be no “one size fits all.”

The chapters in Part II of this book are devoted to these markers. Each is described in greater detail with a focus on the role each plays as a causative agent in atherosclerotic heart and cardiovascular disease. I'll show you how to design your own personalized prevention and/or reversal program using natural, food-derived, nontoxic nutritional medicines that will lower each marker gently back to normal. Retesting at regular intervals will help you track your progress and determine whether your treatment program is working.

I list the cholesterol (lipid panel) first only because it is the most familiar. If I were listing the markers in terms of their predictive capabilities, the lipid panel would come in dead last.

Additional Markers

Identifying and correcting each of these additional markers will further increase your protection from the “Number One Killer”:

- **Blood pressure**—an elevated BP dramatically increases risk of heart attack and stroke.
- **Thyroid Panel**—uncorrected hypothyroidism accelerates atherosclerosis. (More about hypothyroidism [here](#).)
- **Iron Panel**—iron is a powerful oxidizing agent; excess iron has been shown to damage coronary arteries, accelerate atherosclerotic heart disease, promote cancer, and shorten life span.
- **Testosterone**—a low testosterone level (in men and women) increases heart disease risk.

Risk markers versus risk factors

This book is about risk markers. Risk *markers* are measurable biochemicals, present in your blood, that are *causally* associated with atherosclerosis. These risk markers identify the biochemical or molecular *causes* of the disease. Because they provide information about the disruption of normal cellular processes that give rise to atherosclerosis, measuring risk markers provides a rational basis for treatment. If this treatment is instituted at an early stage in the disease process (for example, before symptoms appear), the disease is considered preventable. If treatment is instituted after symptoms appear, the disease is usually still reversible, but accomplishing this is slower and more difficult.

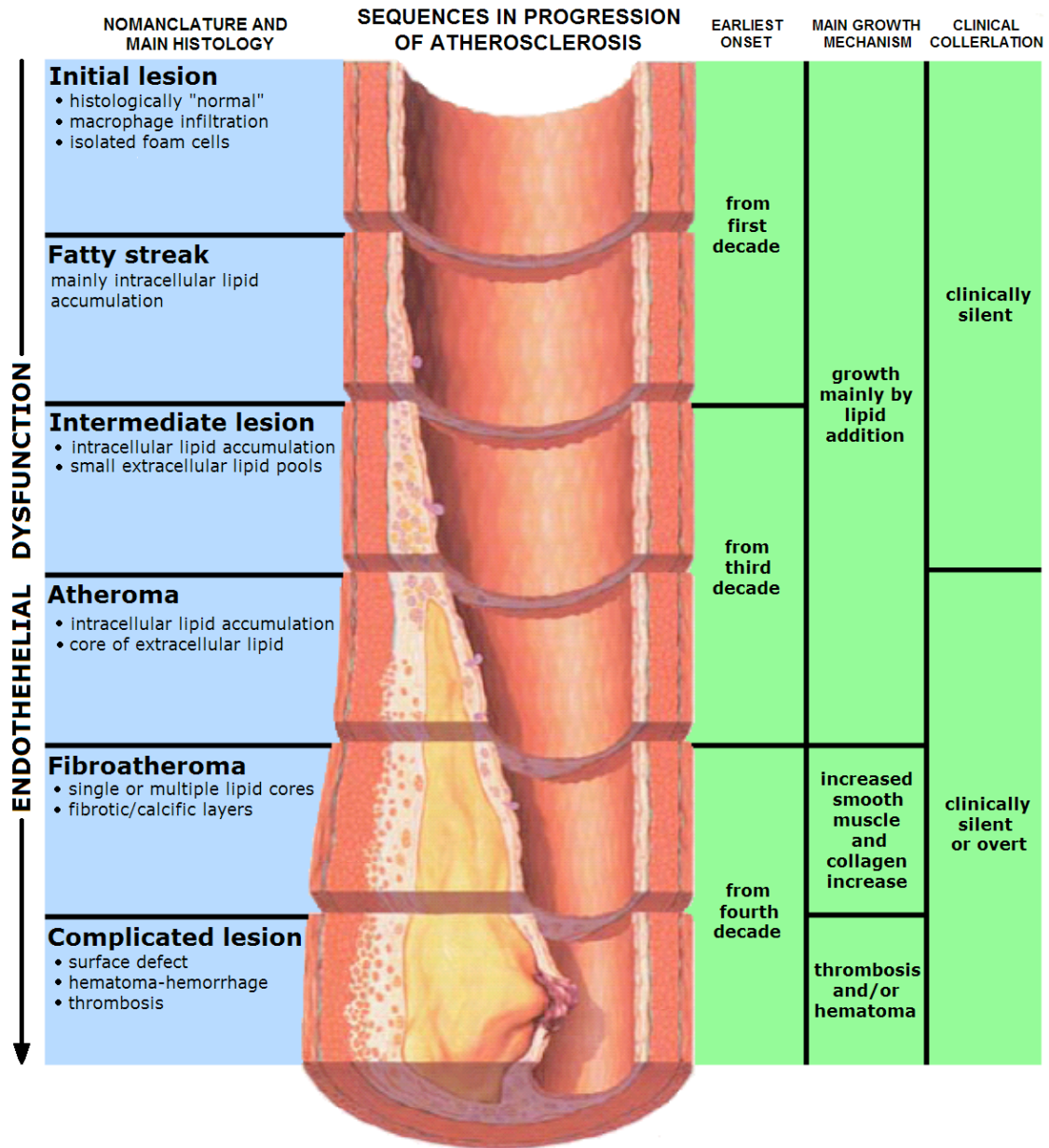
Risk *factors* should not be confused with risk *markers*. Risk factors are behaviors, dietary practices, symptoms, signs, diseases, or genetic predispositions that are associated with *a statistically greater risk* of atherosclerotic cardiovascular disease. These risk factors are based on population statistics, but are not necessarily *causally* related to the disease and therefore have no predictive value beyond statistical probability.

One way of viewing the difference between risk *markers* and risk *factors* is this: If you have a risk *factor* for heart disease, you *might* belong to the group with a higher statistical probability of developing the disease. On the other hand, if you have an abnormal risk *marker*, you *know* that the disease process (in this case, hardening of the arteries leading to stroke and heart attack) is developing in you.

This book is about the six most important risk *markers* for atherosclerotic disease. These tests identify the culprits that actually cause heart attacks and strokes. The following is a list of the known risk *factors* that are statistically—but not necessarily causally—associated with atherosclerotic disease:

Risk *Factors* for atherosclerosis

- Lifestyle
- Sedentary lifestyle/physical inactivity
- Diet high in fat and cholesterol
- Diet high in refined carbohydrates and sugars
- “Junk food” diet (preservatives, additives, processing)
- Animal fat consumption
- Alcohol use
- Stress
- Anabolic steroid use
- Cocaine use
- Smoking in any amount
- Medical history
- Hypertension
- Diabetes mellitus and insulin resistance
- Autoimmune conditions
- Chronic bacterial infection
- Diabetes
- Obesity
- Injury or trauma
- Mercury exposure
- Chemotherapy drugs
- HIV/AIDS drugs
- Viral infections
- Baldness
- Earlobe Crease
- Abdominal obesity
- Family history of premature coronary heart disease
- Congenital heart abnormalities



Progression of atherosclerosis. Atheromas develop gradually. The American Heart Association has identified six stages:

Initial lesion: endothelial damage, macrophage infiltration, foam cell formation

Fatty streak: lipids accumulate and can be observed visually

Intermediate lesion: more lipid accumulation; bigger fatty streaks

Atheroma: further lipid accumulation with extracellular lipid buildup ("core")

Fibroatheroma: multiple lipid cores with addition of fibrotic and calcific layers

Complicated lesion: severe disease, severe lumen shrinkage, hemorrhage, clot formation (thrombosis)

Atherogenesis: How Arteries Fail

Atherosclerosis starts early and develops gradually

My patient, Robert Barnes, is a charming, engaging, and delightfully inquisitive university physics professor. Convinced that knowledge is power, Bob insists that I tell him exactly why his coronary arteries have hardened to the point where he's had a heart attack...

"Doc, I exercise every day, I eat right, and I feel great. My cholesterol is under control. I don't have hypertension. I don't smoke. Every year my internist has been telling me my lipids are great and I have nothing to worry about. So why would I have a heart attack? I know I didn't just wake up last week with heart disease. This must have been developing gradually, right?"

"That's correct, Bob. Even though you had no warning in terms of symptoms, your myocardial infarction didn't happen overnight. The atherosclerotic hardening and plaque formation in your coronary arteries has been progressing gradually and silently for perhaps twenty or thirty years. Until two weeks ago—which was when you felt the chest pain, shortness of breath, and sudden weakness—you weren't aware of anything going on in your heart. The Emergency Room doctor explained that you had suffered a mild coronary—a heart attack. You were admitted for observation overnight, and discharged the next day. Even though the first symptoms were cataclysmic, the process that led up to it had been developing for decades."

"Decades?"

"Yes, several decades. For many victims, coronary hardening and plaque formation begins in childhood. It doesn't surprise me that your doctor didn't know about it. Most doctors don't order the necessary tests, even though it's easy. Nowadays we can identify this killer disease process at the earliest stages and reverse the factors that cause atherosclerosis long before problems arise."

"You can do that?"

"Yes, we can. Welcome to modern molecular medicine, Bob."

"Then tell me why. Why was that happening? What exactly is atherosclerosis, anyway?"

"If you have a few minutes, I'll explain the entire process."

"This is unbelievable! A doctor who explains things to his patients. How refreshing!"

"I have found that patients who understand the origins of their disease are far more likely to succeed at reversing it. Heart patients often go to their doctor hoping to get a magic pill that will somehow make the problem disappear. Physicians encourage this delusion by whipping out their prescription pads, which sends a powerful unspoken message that taking a drug or having surgery will somehow make the problem go away. Though the drugs may help control the symptoms, the underlying problem will not go away unless we identify and remove its causes. So you really need to know how you got into this pickle."

"Makes sense to me."

“It’s important to appreciate how an artery is constructed, so I am going to start with a brief anatomy lesson. Then I’ll explain atherogenesis—that’s the technical term for the development of atherosclerotic plaque. It’s a little complicated, but you’ll be able to follow. Once you have your arterial anatomy down and understand how plaque develops, then I am going to explain how an actual heart attack happens. Later on, you’ll learn how to use biochemical testing to ‘see’ atherosclerosis long before it becomes a problem. Then I’ll show you how to use natural medicines to reverse it.”

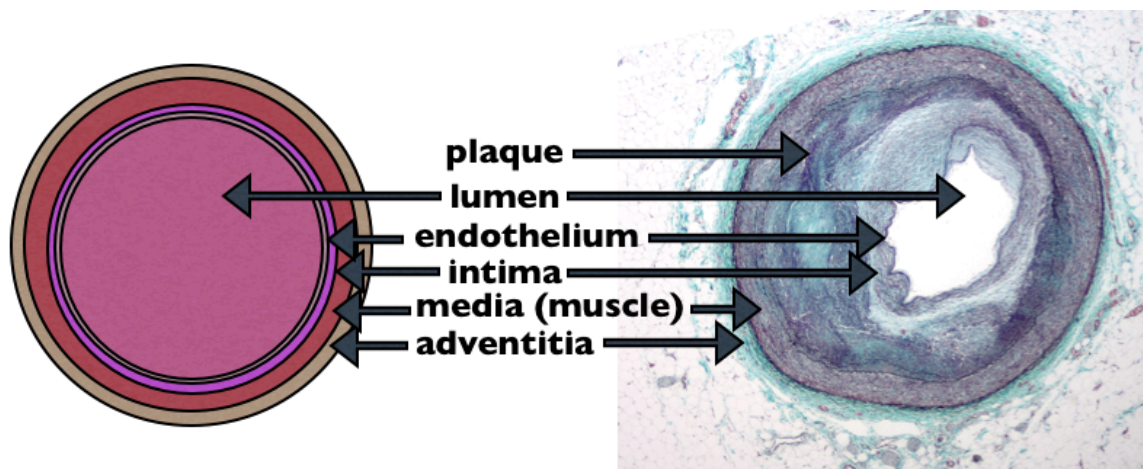
“Doc, you have an organized mind. I like that. Okay, first the anatomy lesson.”

Anatomy of an artery

“Your heart is an amazing organ. It beats more than 100,000 times a day and about two billion times in a life. Your heart pumps five quarts a minute or 2000 gallons a day. Your cardiovascular system—including arteries, capillaries and veins—is over 60,000 miles long, more than twice the distance around the earth.

“An artery is a lot like a very small hose. This particular hose has four layers. Starting from the inside (we call it the “lumen”) and working toward the outside, we’d first encounter a very thin, single layer of cells, called the endothelium. Endo means ‘inner,’ and ‘thelium’ means ‘skin.’ As you will see, the endothelium is the most important part of any artery. This is because of its very special position as an interface—a barrier—that separates the blood flowing through the artery from the wall of the artery. The endothelium is a very selective membrane that allows nutrients and other desirable substances access to the inner layers of the artery while keeping toxins and other undesirables out.

“Beneath the endothelium (working now from the center, or lumen, outward) is a much thicker elastic band of connective tissue called the intima. The intima gives the artery elasticity and flexibility. Beneath the intima (still working from interior to exterior) is the media, a thick layer of muscle cells that contracts to change the size of the artery. And finally, on the outside is the adventitia, an outer protective band of tough elastic fibers that provides structural strength and holds the whole thing together.”



Left: Diagram of normal artery. Right: Microscopic image of a severely atherosclerotic coronary artery.

Phase One: Endothelial injury

“Atherosclerosis, Bob, is the body’s response to vascular injury—or damage to an artery. I am going to show you how this injury happens.”

“Okay.”

“There are four major phases in the development of atherosclerosis and the heart attack and stroke it causes. The first phase is endothelial damage and dysfunction. The second is plaque formation, and the third is thrombus formation.”

“The endothelium,” I continue, “that paper-thin inner lining of your arteries holds the key to understanding heart attacks and coronary artery disease. Atherosclerosis—and all the human misery it causes—begins there. The endothelium’s power is all out of proportion to its size. Just one cell thick, it comprises a very small percentage of the total size of an artery. But, as any real estate agent can tell you, location is everything. Because of its strategic location guarding the interface between blood and artery, the endothelium wields tremendous influence.”

“What can it do?” asks Bob.

“As gatekeeper to the arterial wall, it functions as both a protective barrier and selective membrane. It sorts through all the good and bad chemicals floating in the bloodstream (nutrients, hormones, electrolytes, proteins, cell-signaling molecules, waste material, metabolites, etc.), and decides which to allow through to the arterial wall below. Your endothelium is also a chemical factory: it manufactures special molecules that keep it healthy. And, if it senses damage, it will produce chemical messengers that call in the immune police force.

“Atherosclerosis, The ‘Number One Killer,’ begins when the endothelium is irritated or damaged. This causes it to malfunction, and it can no longer effectively protect the rest of the arterial wall. Oxidized LDL-cholesterol particles flowing through the bloodstream can now penetrate below the injured endothelium and embed themselves in the wall of the artery. Plaque is born.”

"So that's why there's so much emphasis on cholesterol?"

"Yes. Cholesterol is important because if the endothelium is compromised, cholesterol (actually just oxidized LDL particles) will gain entry into the artery, and this initiates and/or accelerates the atherosclerotic process."

“Now let’s imagine we can shrink ourselves down and travel together to the center of one of your coronary arteries, in order to see what happened to the endothelium there.”

“Okay.”

“Unlike the arterial cells beneath it, the endothelium is exposed to everything that flows through the bloodstream, and that bloodstream can carry some very nasty molecular entities. These bang into the endothelium, irritate it, and cause it to become inflamed.”

“Not a good thing?” he offered, tongue in cheek.

“No, Bob, it’s not. Since this is the initial event that leads to atherosclerosis, the disease that kills most of us, I’d say it’s a very bad thing.

“Endothelial irritation is the initial step in a chain reaction that progresses to inflammation, then damage, then dysfunction, atherosclerosis, and finally culminates in a heart attack or stroke.”

“What causes it?”

I opened a book and showed Bob the following list:

Causes of endothelial dysfunction

- insufficient exercise
- high animal fat diet
- high carb diet
- diet low in fruit and vegetables
- depletion of antioxidant nutrients (vitamins E and C, Coenzyme Q-10, etc.)
- pesticides and herbicides in non-organic food
- fast food, junk food, processed food
- air and water pollutants
- chlorination
- smoke
- heavy metals (for example, mercury in fish, lead)
- sugar
- alcohol
- free radicals
- hypertension
- chronic infections such as periodontal disease, Chlamydia, and herpes
- allergies
- autoimmune disease

Preventing endothelial damage

“That’s a long list! Tell me, doc, how can I start protecting my endothelium from damage?”

“Exercise every day, for an hour if possible. I can’t emphasize this strongly enough.

Keeping your blood vessels strong and healthy through exercise is arguably the most important single thing you can do to protect your endothelium from damage.

*“Eat a low-carbohydrate diet: too much sugar and processed carbohydrates are very damaging. Eat organic whenever possible. Keep animal fat at a minimum, because it increases free radical burden. Instead, use moderate amounts of vegetable fat (like coconut, olive, flaxseed, and soy bean oils) along with small servings of very lean meat. Load up on phytonutrient-rich fruit and vegetables. (For a thorough discussion of phytonutrients, see chapter 25 in my book, *Renewal: The Anti-Aging Revolution*.)*

“Every day, make sure you take plenty of nutritional supplements: a multivitamin, extra vitamins C and E, flaxseed oil, and coenzyme Q-10. Antioxidant-rich phytochemical foods and supplements such as pomegranate, blueberries, grapeseed extract, green tea, pycnogenol, milk thistle, and bioflavonoids.

“Some common dietary sources of endothelial irritants include: a high-animal-fat diet, trans-fats, processed foods, chlorinated water, and pesticides.

*“Virtually all chemical toxins irritate and injure the endothelium. Pesticides, herbicides, air and water pollutants, heavy metals (lead, arsenic, mercury, cadmium), tobacco smoke, sugar, and alcohol. Free radicals damage the endothelium. (For a more complete discussion of toxins and free radicals—where they come from and how to manage them—see chapters 2 and 11 in *Renewal*.)*

“Measure and treat (if they’re elevated) the three markers for arterial inflammation: homocysteine, C-reactive protein, and fibrinogen. I’ll have a lot more to say about these rascals later on. For now, I want you to remember that these undesirable irritants cause endothelial

damage, and that lowering your body's level of them will prevent, reverse, and even cure hardening of the arteries.” (See Part II of this book for details about these markers.)

“Okay.” says Bob.

“Blood sugar problems also cause endothelial inflammation. Syndrome X, insulin resistance, excessive insulin, and elevated fasting blood glucose fall into this category. Persistently high blood sugar levels (greater than 90 mg/dL) result in endothelial damage that accelerates atherosclerosis. (For more on this subject see Chapter 11—Blood Sugar, Insulin Resistance, and The Metabolic Syndrome.)

“As a physicist, Bob, you might appreciate that mechanical stress can also trigger endothelial damage. High blood pressure causes excessive “shear stress.” In hypertension, the heart has to beat harder, and this increases the pressure on the endothelial surface and raises the friction caused by blood passing along the endothelium. Because these effects of hypertension are so damaging, it is very important to make sure your blood pressure is normal.

“Several infectious agents are known to damage the endothelium and cause coronary artery disease. These include periodontal (gum) infections, herpes virus, Chlamydia, cytomegalovirus, Helicobacter pylori, and Candida (yeast).

“Allergies and autoimmune diseases (where the immune system makes antibodies that attack one's own tissues) also stir up inflammation that damages the endothelium. Untreated hay fever (allergic rhinitis), sinusitis, asthma, food allergies, rheumatoid arthritis, lupus, multiple sclerosis, and Hashimoto's disease can increase your risk of heart attack.

“Okay, I think I get it now, doc,” says Bob. “Virtually anything that can cause inflammation will damage the endothelium, right?”

“Right. But endothelial inflammation—from some combination of all the causes I just listed—is just the beginning.”

“What happens next?”

Phase Two: plaque formation

“Healthy endothelial cells protect the intima, the layer of arterial wall that lies beneath. When the fires of inflammation have damaged endothelial integrity, however, LDL particles now can gain access to the intima.”

“Aha!” says Bob. “So the LDLs get into this place where they don't belong. That's why they cause such big problems. I've always wondered about that.”

“You're right, but it's a bit more complicated. As they become trapped between the endothelium and the intima, LDLs are oxidized by the free radicals that were generated by the local inflammatory reaction. In response to the oxidized LDL, the inflamed endothelium senses danger, goes into ‘alarm mode’.”

“Alarm mode?” asks Bob.

“Endothelial cells manufacture and release messenger molecules that tell the immune system to send in its monocyte cells. Monocytes, a kind of white blood cell, are the cellular police force.”

“How are they like cops?”

“Several ways. They are mobile, attracted to problem areas, carry weapons—and they have an ‘attitude.’ Their job is to take over and control situations they deem “dangerous” (real or perceived). Monocytes can use their communication system to call in reserves if needed. An

inflamed blood vessel wall like the one I've been describing, coupled with some oxidized LDL, is definitely perceived as a dangerous situation.

"Under normal conditions," I continued, "monocytes in the bloodstream, like police on patrol, would have just slid on by, but now they migrate toward and adhere to this sticky inflamed endothelial surface. Then, on the trail of the oxidized LDL, they, too, go through and below the endothelial cell and embed themselves in the intima."

"In pursuit of perps?" offers Bob.

"Yes, but now things get weird. Once safely beneath the surface layer of endothelial cells, these monocytes do something real cops could never do: they rapidly increase their size by several times, transforming into another type of white blood cell, the macrophage."

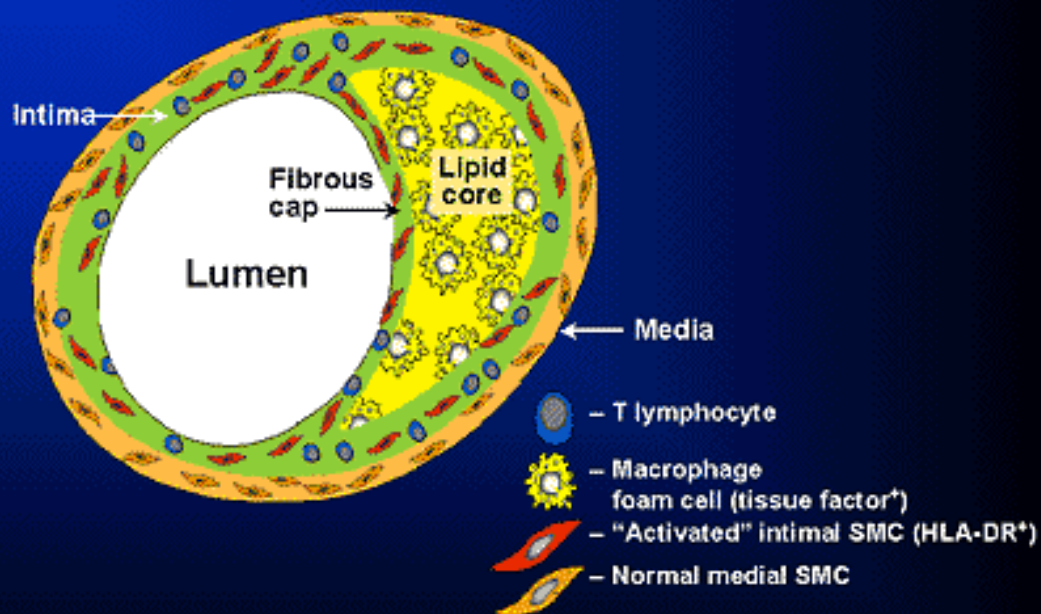
"Okay, I'll bite—what's a macrophage?"

"Macrophages are a kind of huge immune system supercop cell. Their enormous size allows them to more easily engulf things, and when they are munching on toxins and viruses, on fungal cells and cancer cells, we are very happy with their behavior. But just like good cops gone bad, when they get into the inside of your blood vessels and start gobbling up cholesterol and oxidized LDL...well, we have a friendly fire situation. They do more harm than good.

"They actually eat the oxidized LDL?" asks Bob.

"Yes. We call it 'phagocytosis.' Here's how it works: a macrophage snuggles up to one of the LDLs, and then sends out two 'arms' of protoplasm that surround it in a deadly hug, and then close in from behind, totally engulfing it, so that now the LDL is actually completely inside of the macrophage. Instead of simply gobbling up a few of the oxidized LDLs and digesting them, however, these macrophages overindulge; they can't stop eating, so they become engorged with fat. The fat that they have been eating, however, is lethal to them. They die, but not before they grow so large that they can't get back out of the arterial wall, so they become entombed there. The LDL-engorged carcasses of these dead macrophage supercops accumulate in the intima, and consolidate to form plaque. On a microscopic slide preparation these dead cells take on a bubbly appearance, and have come to be called 'foam cells.' When sufficiently large numbers of foam cells accumulate, fatty yellow streaks appear. These protrude above the interior surface of the artery into its lumen; this narrows the vessel and reduces its capacity to carry blood. We call this ischemia. Ischemia in brain blood vessels causes cognitive problems. Ischemia in heart vessels causes chest pain, fatigue, and shortness of breath. And, of course with atherosclerotic blockage you have increased risk of heart attacks and strokes."

The Anatomy of Atherosclerotic Plaque



Libby P. *Lancet*. 1996;348:S4-S7.

Anatomy of atherosclerotic plaque. The work of Peter Libby and colleagues has demonstrated that plaques with a large lipid core and a thin fibrous cap are more likely to rupture.

Phase Three: thrombus formation, rupture, and disaster

"So that's the end of the second phase, which you called plaque formation?"

"Right, Bob. The third and final phase is thrombus formation."

"I guess it really is 'final' for some people."

"Bad joke, Bob. But sadly, it's true. You've probably also heard this one: 'The first symptom of a heart attack is often sudden death.' This is the unfortunate truth for about half of all heart attack victims."

"Now that you have my attention, exactly what is a 'thrombus,' doc?"

"It is simply a blood clot—a very dangerous kind of clot that occurs inside an artery. But we are getting ahead of ourselves. First you need to know about unstable plaque. On the way to eventually becoming 'stable plaque,' these fatty atherosclerotic deposits go through a dangerous phase known as 'unstable plaque,' in which a very thin layer of connective tissue cells forms a thin, fibrous cap that covers over the fatty plaque lesions I've been describing. It's a lot like the thin scab that you can see soon after an external cut or scrape on your skin. This cap sits on top of the foam cells in the fatty streak, forming a 'bump' that protrudes even further into the lumen (the inside) of the vessel."

"Calcium," I continued, "is now attracted to the area and deposits there, causing the plaque to harden, or 'calcify.' This causes the plaque to gradually become less elastic and more brittle, like thin bone, and it can now easily break."

“This combination of foam cells, calcification, and lipids, covered over by a fibrous cap, is what we call ‘unstable plaque.’ It’s kind of like a festering sore, or boil, and it’s especially dangerous, because, as you can see, the normally soft and pliant connective tissue “cap” that covers it has now become hard, fragile, and brittle.

“Beneath this fibrous cap,” I continued, “trapped foam cells are dying and in their death throes they release harmful chemicals that push upward, encouraging the fibrous cap to rupture. If the cap does rupture, all heck breaks loose. It’s like a pimple or boil erupting: toxic contents are spewed out. A clot, or thrombus, starts forming right there on the inside wall of the artery. If this clot becomes large enough, it will cause local blockage of downstream blood flow (called an ‘infarction’) in the affected artery. Or the developing clot can break loose and travel downstream, quickly lodging in a narrower portion of the artery. Either way, this is what we call a cardiovascular ‘event.’ If this ‘event’ occurs in the heart, it’s a myocardial infarction. The victim suffers sudden chest pain, fainting—and as often as not, death. If the blockage happens in the brain, we call it a stroke, or cerebral infarction and the patient suffers loss of cerebral function or death.

“This complex atherosclerotic process I’ve just described usually remains silent—in other words, there are no symptoms. And without symptoms, there’s no way to know it is developing. No medical procedure or imaging technique can detect an unstable plaque on the verge of rupture. Nothing like a heart attack attention.”

“I can vouch for that! But now we have a way to know that train wreck is coming. Now we can do the six tests you recommend.”

“Right, Bob.”

“And then we can use your molecular medicine program to reverse the causes of heart attacks before they happen?”

“You are a perceptive fellow, I must say! Now, thanks to these new discoveries, long before disaster strikes we can use our knowledge of cellular and molecular biology to prevent this disease. If we do our molecular homework, there’ll be no reason for plaque to form and rupture, causing these cataclysmic, life-changing—and often life-ending—events. Get tested! Find those biochemical signs of plaque development! Nip this disease in the bud.”

“That’s why I’m here, Dr. Tim. To learn how to do that. Thanks for the explanation.”

“Anytime.”



Horizontal section through a heart showing infarction of left anterior ventricular wall. (You are looking upward. Top of illustration is front of body.)

Chapter 6

How to Get Tested and Design Your Heart Program

The Cardiovascular Risk Marker Panel

These are the six tests you need to evaluate cardiovascular risk:

- **Lipid Panel** (cholesterol, triglycerides, LDL, HDL)
- **C-Reactive Protein** (cardiac or high sensitivity)
- **Homocysteine, plasma**
- **Fibrinogen** (activity, *not* antibody)
- **Fasting Glucose**
- **LDL Particle Size**

How and where to get tested

The tests I recommend in this book are not exotic or unusual. They can be done by any qualified medical laboratory.

If your insurance doesn't cover testing and you are paying out of pocket, use [DirectLabs](#) for all testing. Direct Labs offers the highest quality testing at a reasonable price. To order the six tests I recommend, click on the Tim Smith, MD Panel. Current price is \$189. (You may want to consider adding the Special Thyroid Panel, Iron Panel, and Testosterone Free and Total.)

If you do have insurance coverage, but with a high deductible, use [DirectLabs](#).

If your insurance does cover testing, take the list of six tests (lipid panel, C-reactive protein, homocysteine, fibrinogen, fasting glucose, and LDL particle size profile) to your doctor and ask him or her to order them for you. Expect some resistance. Most doctors are not up to date on the latest cardiovascular research findings. Chances are they won't appreciate the importance of these tests. They may even have a bit of an attitude about it. You may be told that these newer tests are still "experimental," or "unproven," or "unnecessary," and "all you really need is a lipid panel."

If your doctor does agree to order these tests, it is unlikely that (other than cholesterol) he or she will know how to interpret and/or treat abnormal results. Though many hardheaded physicians believe they learned everything they need to know in medical school, there are some flexible souls out there who truly want to learn and grow and apply the latest research findings. If your doctor is one of these, it might help to provide them with a copy of this book.

If you need help with any aspect of testing or interpretation, including finding a local physician who understands the principles outlined here, contact me at drsmith@renewalresearch.com.

If you are a physician who supports an enlightened approach to cardiovascular disease, please contact me at drsmith@renewalresearch.com. There are patients out there who need you!

Insurance coverage and low-cost testing

If you have PPO (preferred provider organization) health care insurance, chances are excellent that all the tests will be covered.

Because deductibles can be high and other labs charge much higher rates than [DirectLabs](#), using your insurance—even with coverage—may not be the most cost-effective option. Compare prices!

If you have an HMO, expect a hassle from your "gatekeeper" doctor. Insurance company HMOs don't like their doctors to order too many tests, so they penalize the ones who do. HMOs are not into prevention; they are more concerned about cutting short-term costs. It won't hurt to ask, but you will almost certainly be told that these tests aren't covered. If this is the case, go to [DirectLabs](#) or contact me at drsmith@renewalresearch.com for more information.

Medicare covers all the tests I recommend—so long as you haven't signed your wonderful “original Medicare” coverage over to an HMO. (*Don't do that!*)

When your results come back

For each abnormal (out-of-range) results, read the corresponding chapter in Part II of this book. For example, if your CRP and fibrinogen are elevated, read Chapter 8 about CRP and Chapter 10 about fibrinogen. Of course, I'd be honored if you read all the chapters, but you really only need to read the ones that pertain to your abnormal test results.

About normal ranges

Important note: The normal ranges listed on your lab test printout are often **inaccurate** (that is to say, not consistent with the latest research literature). **Do not use them! Follow the normal ranges provided below and in this book.**

Allow me to provide a couple of examples. A typical lab printout will give the normal range for homocysteine as “0-13.0 umol/L.” The research literature tells us, however, that heart attack risk starts at a homocysteine of 5, and has doubled in those with a level of 10. At 13 the probability of a coronary event is 250% of baseline! Obviously, an individual with a homocysteine of 13 is at high risk.

Another example: Recently one of my patients received a lab printout that gave the normal range for fibrinogen as “208-423 mg/dL.” Her level looked normal at 352. However, the research literature shows that cardiovascular event risk begins at 250, and is 2-3 times higher by the time you get to 352.

The two situations where the labs and I agree are cholesterol (including the entire lipid panel) and LDL Particle Size. Lab normals for the other four markers—C-Reactive Protein, Homocysteine, Fibrinogen, and Fasting Glucose—are usually at variance with the current literature.

Normal ranges for all markers are provided in the bulleted list below and in the respective chapters:

- Cholesterol ≤ 200 , LDL < 99 , Triglycerides < 150 mg/dL, HDL > 40 , or VLDL < 30 .
- C-Reactive Protein 0.0-0.8.
- Homocysteine ≤ 6.3 .
- Fibrinogen (activity) 150-250.
- Fasting Glucose ≤ 90 .
- LDL Pattern: A.

Additional markers:

- Thyroid Panel (“Special Thyroid Panel” at [DirectLabs](#)): Free T3 (3.5-5.5 is optimum), Free T4 (0.9-1.9), TSH (≤ 1.5).
- Iron Panel—iron level with TIBC (total iron binding capacity) and ferritin (use lab normals).
- Testosterone, Total (Ideal range 50-150) and Free (6-18).

Interpret your test results and design your program

Remember, *each abnormal result tells you atherosclerotic disease is developing in your arteries right now*. Reversing that abnormal result will reverse the disease process.

For each of your markers that is outside the normal range: 1.) read the relevant chapter (see list below), and 2.) follow the recommended program:

- If you have an abnormal Cholesterol (≥ 200), LDL (> 99), Triglycerides (> 150 mg/dL), HDL (< 40), or VLDL (> 30 mg/dl, read Chapter 7—**Lipoproteins and the Lipid Panel: Cholesterol and LDL, Triglycerides, HDL, VLDL**.
- If you have an abnormally high C-Reactive Protein (> 0.8), read Chapter 8—C-Reactive Protein.
- If you have an abnormally high Homocysteine (> 6.3), read Chapter 9—Homocysteine.
- If you have an abnormally high Fibrinogen (> 250), read Chapter 10—Fibrinogen.
- If you have an abnormally high Fasting Glucose level, (> 90), read Chapter 11—Blood Sugar, Insulin Resistance, and The Metabolic Syndrome.
- If your LDL particle size is Type B or “mixed” Type A and Type B, read Chapter 12—LDL Particle Size.
- If your thyroid level is low, you will need to [seek treatment](#). Also, to better understand this condition, read Chapter 36 of my book, *Renewal: the Anti-Aging Revolution*. (Rodale Press and St. Martin’s Press).
- If your iron level is high, donate a unit of blood to bring it down.
- If your testosterone level is low, find an alternative-minded doctor who will prescribe testosterone. For information about the importance of testosterone read Chapter 35 in *Renewal*. For information and referrals call Women’s International Pharmacy at 1-800-279-5708.

Using the information provided in the appropriate chapters, design your own personal program. To make this process easier, I’ve provided numerous dietary, lifestyle, and nutritional medicine options that work to normalize each marker. These are not casual or random recommendations; *every item I’ve listed has been proven effective in peer-reviewed published research studies*. The nutritional medicines I recommend are widely used by today’s alternative and integrative physicians. *The more of these recommendations you can follow, the better your outcome will be.*

Follow-up testing is crucial to your success

Repeat testing at regular intervals is the only way you will know whether your program is working. Here is the schedule I recommend:

After 8-12 weeks, retest

Once you have chosen the elements of your program, follow it consistently. Take your supplements twice a day, *every day*. Follow your diet *every day*. Exercise for a full hour *every day*, if you possibly can. Then, after two to three months, it’s time to retest. You only need to retest the markers that had been abnormal on initial testing.

These results are your guide to adjusting your program. Don't be disappointed if your markers have not yet become normal. The purpose of testing at this point is simply to make sure that you don't continue too long on a program that is not working. Your program will take from 6-12 months or more to have its full effect, so the results you get on the first follow-up test are unlikely to be ideal. We are simply looking to make sure that you are *moving in the right direction*.

If your numbers indicate improvement—even if it is modest—continue on your program. If you have followed your program carefully and the number for any given marker hasn't budged (or is higher), then you do need to try different options. Otherwise, stay the course, while reminding yourself that *this is a gradual process*.

We are all metabolically and biochemically different. Therefore, some nutritional medicines will work for you that might not work for others, and vice versa. That's why I have listed many different options (all supported by the research literature) for treating each marker. If your initial program does not seem to be working, don't give up, just switch to other options. Although I expect the top-ranked options to work for more people more of the time, only trial and error coupled with repeat testing will determine the program that works best for you. Again, for each marker that is moving (however gradually) in the right direction, just keep doing what you have been doing. If any marker is not moving toward normal, study the list of recommendations for that marker and change your program.

Continue testing each abnormal marker every three months until it becomes normal

To make sure your program is working, it is necessary to retest at *three-month* intervals until you find the combination of supplements that works best for you. Continue to adjust your program and retest until your abnormal markers are all consistently moving toward the normal range.

After all of your elevated risk factors have moved into the normal range, *retest all the markers (not just the ones that have been abnormal) every six months* to make sure they stay there.

Additional risk markers for cardiovascular disease

- **Hypertension**—If your blood pressure is above 135/85, it is important to get it down into the normal range (ideally 120/80). Hypertension damages arteries and accelerates atherosclerosis. Use natural treatments if possible. Treating hypertension is a complex topic and beyond the scope of this book. Daily exercise is a crucial natural tool for reversing elevated blood pressure.
- **Hypothyroidism**. Thyroid hormone is an anti-aging hormone, so you want optimum amounts to both feel good and live long. Doctors frequently fail to correctly identify hypothyroidism. Common symptoms of hypothyroidism include fatigue, temperature intolerance, constipation, dry skin, cold extremities, and inability to lose weight. Even a marginally under-active thyroid gland predisposes to atherosclerotic coronary artery disease. For more information, a list of symptoms, and information about testing your basal temperature at home to diagnose possible hypothyroidism see Chapter 37 in my book, *Renewal: The Anti-Aging Revolution*. Three tests are required to make this diagnosis: **TSH, Free T-3, and Free T-4**. Ideal ranges: Free T-3, 3.5-5.5 pg/ml; Free

T4, 0.9-1.9 pg/ml; TSH, less than 1.5 mIU/L. If your TSH is above 2.0 or your Free T3 is below 3.5, you are hypothyroid.

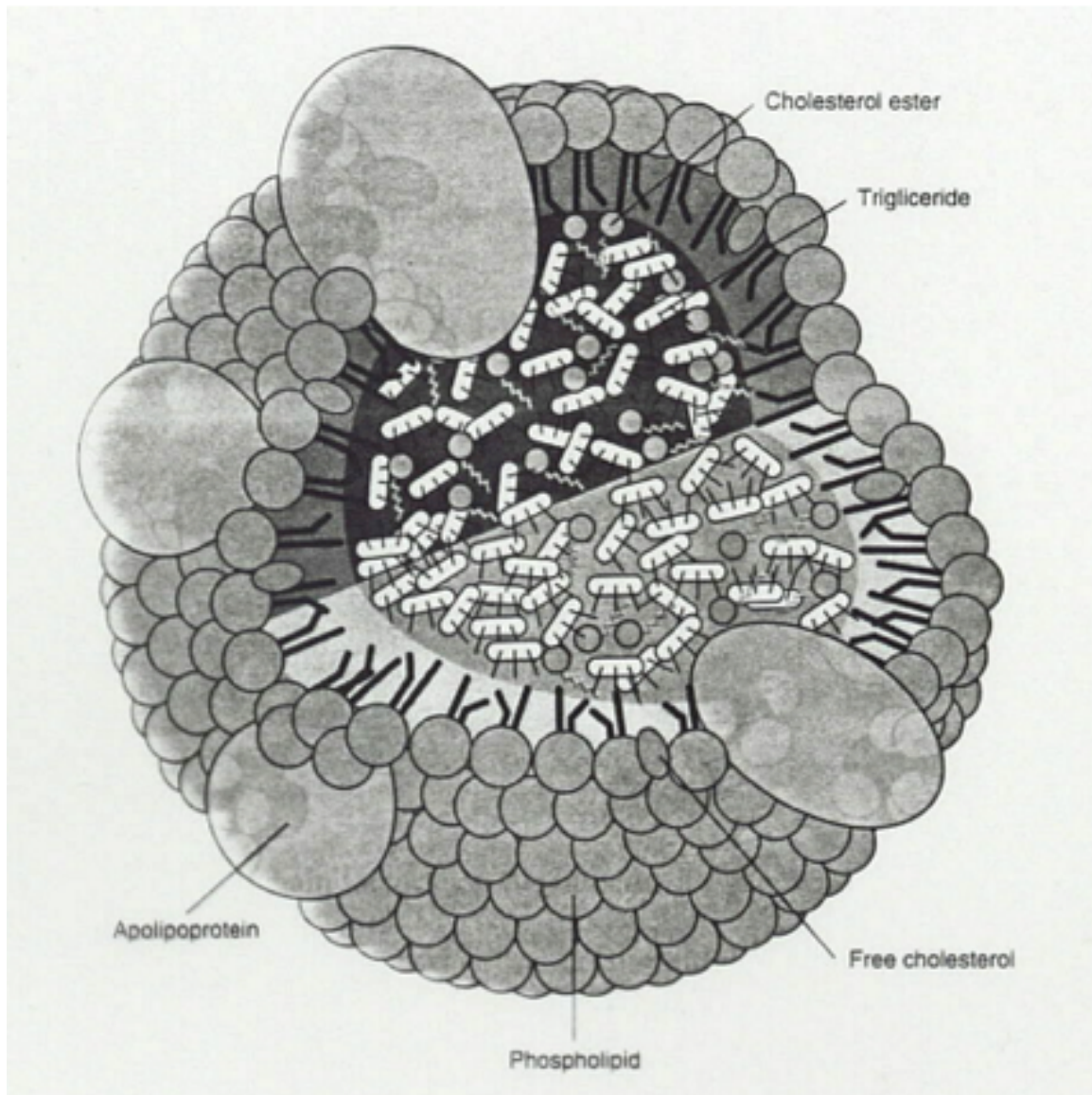
- **Iron Panel**—Because iron is a free radical and a powerful oxidizing agent, excesses overload the body's antioxidant systems, increasing the risk of heart disease and cancer. An iron panel usually includes **serum ferritin** (the primary protein used for iron storage), **serum iron**, **total iron-binding capacity (TIBC)**, your red blood cells' capacity to transport iron), and **transferrin** (a protein that binds iron).
- **Testosterone**—Low testosterone levels (in men and women) increase heart disease risk. Ask for a **free and total testosterone level**. Ideal total testosterone range for men is 300-1500; for women 50-150.
- **Chlamydia pneumoniae, Helicobacter pylori, and Cytomegalovirus antibody levels** (IgG, IgM). These microbes have been shown to cause and/or accelerate progression of atherosclerotic coronary artery disease.

A note about supplements

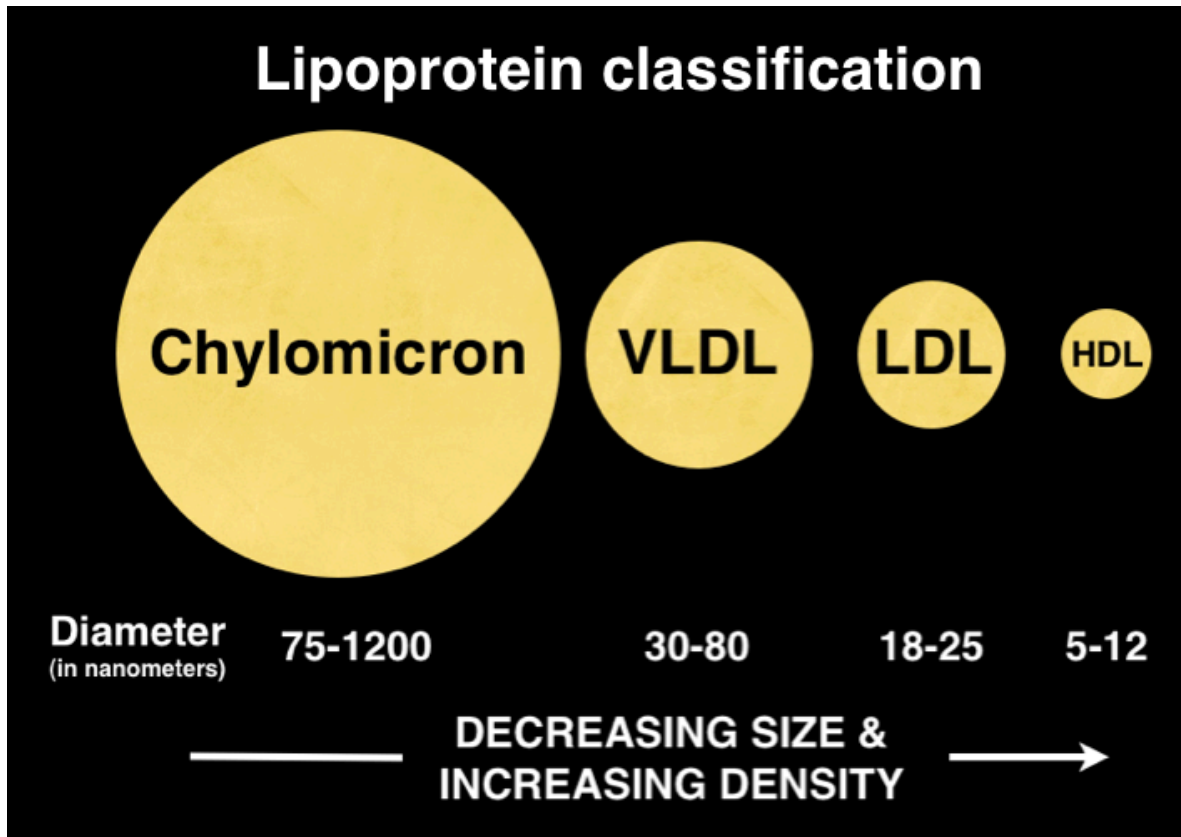
The importance of avoiding low quality nutritional supplement products cannot be overemphasized. These products can make you sick because they contain inferior and/or toxic source material. Supplements from any national drugstore and supermarket chain, or any big box store (even the ones we have come to trust for quality in other areas, such as food, pharmaceuticals, or other consumer products), virtually always contain low quality, often toxic source material, and unwanted additives. Companies whose products I do recommend include [Renewal Research](#) (disclaimer: the author is founder and part owner of this company), ProThera, Thorne Research, Allergy Research Group/Nutricology, Ecological Formulas/Cardiovascular Research, Solgar, Phytopharmica, Intensive Nutrition, and Pure Encapsulations.

In Part Two II I'll discuss the personality of each heart marker, how it participates in the atherosclerotic disease process, and what you need to do if yours comes back abnormal...

Part Two: The Markers



Structure of a lipoprotein particle. The outer coat contains free cholesterol, phospholipids and proteins (Apolipoproteins) that assist LDL transport in the blood. The core contains cholesterol ester and triglyceride molecules.



Relative sizes of lipoproteins.

Chapter 7

The Lipid Panel

Cholesterol, LDL, Triglycerides, HDL, VLDL

Lipoproteins

Everything we eat is composed of just three types of nutrients: fat, protein, and carbohydrate. The proteins (digested down into individual amino acids) and the carbohydrates (digested down into individual sugar molecules) are soluble in water, and so can be easily shipped through the bloodstream. Fats, on the other hand, are not water soluble, so Nature had to find a way to package up in order to ship them around in the body. Lipoproteins, specialized

water-soluble particles that enable lipid transport, are the “solution” to this problem. Synthesized in the liver, lipoproteins solubilize lipids, ferry them about to the far reaches of the body, and then unload them at specific target sites.

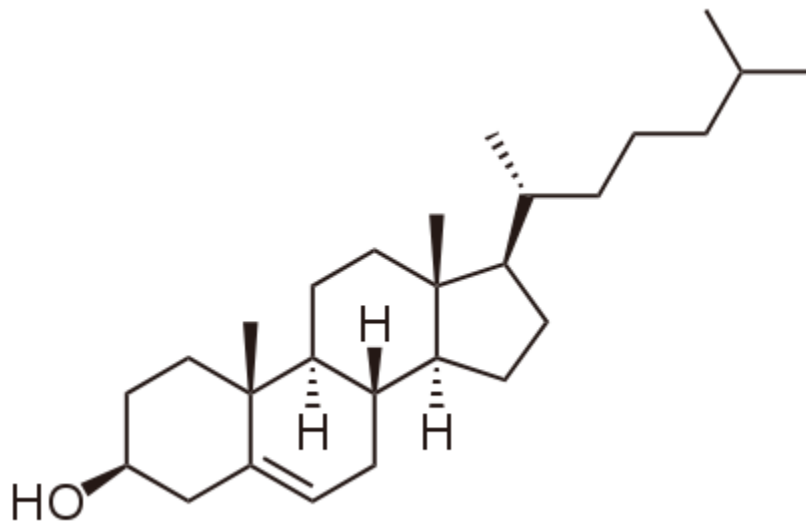
Though there are many types of lipoproteins, the three most important ones are found on a standard lipid panel: LDL, HDL, and VLDL.

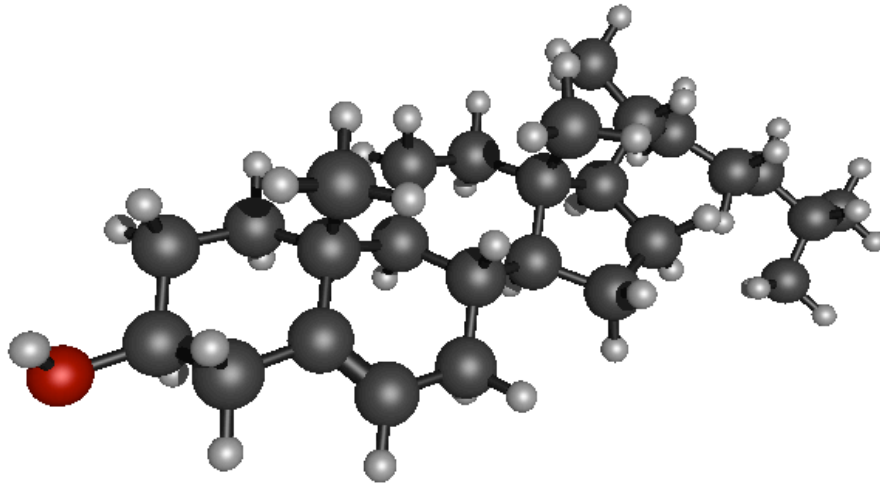
Lipoproteins are tiny, nanoscale balls whose outer wall is a single layer of fat (phospholipids and cholesterol) with protein molecules embedded in it. The inner contents—the payload, if you will—of lipoproteins includes cholesterol, triglycerides, and small amounts of other lipids.

Lipoproteins come in a variety of sizes, ranging from very small to very large. Of course my use of the word “large” here is relative; all lipoproteins are tiny. We measure their size in nanometers (nm), or billionths of a meter.

HDL (high density lipoprotein) particles are the smallest lipoproteins. They range from 5-12 nm in diameter. LDL particles are somewhat larger, averaging 18-25 nm, and VLDL (very low density lipoproteins) are the largest of all, averaging 30-80 nm in diameter.

If an HDL particle were the size of a softball, LDL particles would be the size of a soccer ball and VLDLs would be the size of a beach ball. The triglycerides carried around inside these lipoprotein particles would be marble-sized and the cholesterol molecules would be the size of a pea.





Molecular structure of the cholesterol molecule—2 dimensions above; 3-D below.

Components of a Lipid Panel

- **Total Cholesterol**
- **LDL (Low Density Lipoprotein)**
- **Triglycerides**
- **HDL (High Density Lipoprotein)**
- **VLDL (Very Low Density Lipoprotein)**

In the following sections I'll discuss each component of the Lipid Panel. And if your numbers are off, you'll learn how to fix them.

Cholesterol: Good or Evil?

Cholesterol's image problem

What's the first thing you think of when you hear the word "cholesterol"? Most folks associate the word with disappointing outcomes: heart attacks, strokes, hardening of the arteries, bypass surgery. It might surprise you to learn that cholesterol is actually a good guy, a steroid-type molecule that is crucial to our existence. Without cholesterol, life as we know it would be impossible. So allow me to tell you a little more about cholesterol, a molecule no less necessary for optimum health than vitamin C and insulin.

Synthesized in the liver and most other body tissues, cholesterol is a relatively simple molecular building block used by our bodies to manufacture hundreds of other molecules.

Cholesterol is a crucial structural component of the walls that surround every one of your 100 or so trillion cells.

We'd be hard put to reproduce our species without the estrogen, progesterone, testosterone, and hundreds of other steroid hormones manufactured from cholesterol in our ovaries and testes.

In the adrenal glands, cholesterol is the starting point for synthesis of over 150 stress management hormones (including pregnenolone, DHEA, cortisol, etc.). These steroids manage stress and inflammation (for example, allergies, infections, trauma) and immune responsiveness.

The liver transforms cholesterol into bile juices that are delivered to the intestinal tract to digest and absorb fats. Without this form of cholesterol, we would be unable to absorb the essential fatty acids and fat soluble vitamins (A, D, E, and K) from food and supplements.

In the skin, ultraviolet light transforms cholesterol into vitamin D (which is also a hormone). Recent research has shown vitamin D to be far more important than we originally imagined. Beyond its role in calcium metabolism and bone health, D is now known to play critical roles in mental health, blood sugar regulation, immune health and cancer prevention.

Without cholesterol, we'd be in big trouble: we'd have no protection from stress, no sex life, nothing to keep our cells from falling apart, our risk of degenerative disease would skyrocket, cancer would be far more prevalent, and we'd die young. So cholesterol can't be *all* bad.

If cholesterol does so many good things, why does it have such a lousy reputation? Let's face it: elevated cholesterol is intimately associated with high risk of heart attack and stroke, so most people think of it as a kind of molecular mass murderer. Millions of human deaths every year can be traced directly back to elevated blood levels of this waxy molecule. How could a substance so important to our well-being have gone so far astray? To answer this question, you need to know a little more about cholesterol and LDL, its partner in crime.

Where does Cholesterol come from?

There are only two ways cholesterol can get into your body (and from there into the bloodstream and perhaps deposited as plaque in the walls of your arteries):

1. You eat it, by consuming animal-derived foods (plant foods contain no cholesterol).
2. Your liver makes it.

First let's consider the outside sources—the dietary sources—of cholesterol. The amount of cholesterol we *eat* is determined solely by the amount of animal food we consume. *All animal foods* (seafood, beef, poultry, eggs, dairy) contain cholesterol. *No plant food* (fruit, vegetables, grains, beans, nuts, seeds) contains cholesterol. So those who choose to eat vegetarian are automatically on a cholesterol-free diet.

The amount of cholesterol we *make* is genetically determined, and varies greatly from one person to the next. That's why some people—the ones who are programmed not to make much cholesterol—can easily lower their blood level by simply reducing the amount of cholesterol-laden animal foods they eat. Dietary restriction works for this group because their extra cholesterol is all coming from diet.

Others, however—and I am a card-carrying member of this group—are genetically programmed to make lots of cholesterol, regardless of how much we consume. We find it

impossible to lower our cholesterol by simply restricting animal foods. Even if we eat a vegan (cholesterol free) diet, our bodies just ramp up the cholesterol-manufacturing machinery to make up for the shortfall. In my case (and I am definitely not alone), without treatment, my cholesterol stays at the same high level—regardless of whether I eat vegan.

Many years ago so I tried a little experiment on myself. For one month I ate a high animal fat diet. We are talking eggs with butter for breakfast, burgers for lunch and ham or steak or chicken for dinner. Then I checked my cholesterol and it was very high at 305 (normal is less than 200). For the next month, I switched to a strict vegan diet that contained no animal foods and thus no cholesterol. If cholesterol was present, my body had to be making all of it. The lipid panel at the end of the second month was exactly the same as the one at the end of the first: 305!

My experiment demonstrated that for members of the genetically predisposed high-cholesterol group (like me), dietary cholesterol restriction (that is, avoiding animal fats) won't work. We need a more stringent program that includes the following:

- daily exercise
- very low total carbohydrate intake
- sugar restriction
- minimal animal fats (very lean meat, nonfat dairy)
- red yeast rice extract (the original, only natural—and by far the best—statin)
- pomegranate juice (fresh, organic)
- curcumin (turmeric)—for optimum absorption use Meriva® phytosome bound form
- garlic (as the fresh vegetable or in capsules)
- other natural cholesterol-lowering agents (see information at the end of this chapter)

Cholesterol transport into the cell

When a cell needs some cholesterol (remember that all cells need cholesterol and it serves many functions in the body), that cell's DNA synthesizes LDL receptor proteins that migrate to the outer cell membrane and become embedded in it, causing the formation of a small receptor "pit." The LDL receptor then sends out signals that entice nearby LDL particles, and when one gets close, the receptor snares it. The receptor protein, along with its cholesterol-laden LDL particle, then forms a small vesicle that moves to the interior of the cell and merges with another membrane-bound sack called a lysosome. The lysosome secretes enzymes that separate the cholesterol from the LDL particle. The cholesterol is released into the cell and the LDL receptors are recycled back to the outer cell membrane where they latch onto another LDL particle and repeat the process.

Cholesterol: a weak marker for atherosclerotic disease

Unlike all the other markers described in this book, cholesterol is an "innocent bystander," the molecular guy who happens to be in the wrong place at the wrong time. Let me explain. Because LDLs contain cholesterol, their numbers go up and down in tandem. Too many LDLs will therefore always translate into too much cholesterol. Cholesterol does not by itself cause vascular disease. It just happens to be inside of the LDL particles that (when oxidized and then devoured by macrophages) end up trapped in plaque in the walls of arteries. (For a more complete explanation of this process, see Chapter 5: Atherogenesis.)

LDL: Little Balls of Fat

LDLs are lipoprotein particles that function like miniature trucks. Their payload is cholesterol. Each LDL particle packs about a thousand cholesterol molecules inside its greasy outer coating and carries them from the liver to various locations around the body. Once delivered, the cholesterol is dropped off and converted into the array of biochemicals listed above: hormones, cell walls, digestive juices, vitamin D, etc.

Why LDL is important—the Cholesterol-atherosclerosis connection

Evidence from a very large body of research supports the notion of a close relationship between heart attacks and an elevated LDL level. Of thousands of studies, perhaps the best-known and most convincing is the Framingham long-term population study of heart disease risk, which tracked medical data and habits (dietary, exercise, smoking, etc.) of thousands of citizens of a small Massachusetts community for over five decades. Specifically, the Framingham study showed that people with elevated cholesterol levels experienced more heart attacks. This population study correlates tightly with basic science research showing that animals with experimentally induced high cholesterol levels develop atherosclerotic lesions indistinguishable from those found in humans. So, there's really no need to question that cholesterol is the bad guy, right? Well, not so fast...

Oxidized LDL—the real culprit

It turns out that the true villain *isn't* cholesterol, or even LDL. It is *LDL oxidation*. LDL particles in their *unoxidized* form present no danger to our arteries. If the LDL becomes oxidized, however, trouble is brewing. LDL particles can easily become oxidized in people with an excess of free radicals (too much junk and processed food, pesticides, pollutants, toxins, etc.) or those with a deficiency of antioxidants.

In the oxidized state, LDL has become a free radical that damages (again, by oxidation) that delicate inner arterial lining, the endothelium (see Chapter 4). Having caused local endothelial irritation and inflammation, the oxidized LDL particle can now find its way through and beneath the endothelium. Once there, it can't get out, so it accumulates, and this accumulation eventually becomes what we know as atherosclerotic plaque.

So it's *oxidized LDL*—not cholesterol—that's responsible for the millions of deaths every year from heart and cardiovascular disease. For decades now we have been looking at the cholesterol “innocent bystander” rather than at *oxidized LDL*. Cholesterol served as an adequate marker because it tracks LDL and LDL, in turn, is directly proportional to oxidized LDL. Oxidized LDL alone, however, provides a far more accurate marker for predicting cardiovascular “events.” Unfortunately, oxidized LDL testing is currently not available, but hopefully that will change as increasing numbers of doctors and researchers come to appreciate its powerful causative role.

Now it becomes clear why cholesterol and LDL are weak markers. The people with high LDL and high cholesterol who never have a heart attack are the ones with lower levels of *oxidized* LDL.

Size matters too

Recent studies have shown that LDL *particle size* correlates with atherosclerosis progression far better than the actual *number* of LDL particles. Smaller, denser LDL particles are dangerous because they can more easily squeeze between endothelial cells and gain access to the wall of the artery, where they cause plaque formation. Larger LDLs can't get through, so they are associated with a great degree of safety. High concentrations of small LDL particles are associated with higher rates of cardiovascular events (heart attacks and strokes), faster progression of atherosclerosis, and higher risk of death. Conversely, high levels of large, buoyant, "fluffy" LDL particles confers great protection. See Chapter 12 for more about LDL density.

Unstable plaque: exceptionally dangerous

Recently formed plaque is a waxy deposit that causes a bulge on the inside wall of a blood vessel. Plaque is an inflammatory process that is going through the initial stages of healing. Like a pimple or a boil, this early plaque lesion is covered by a scab-like affair: a very thin, fragile layer of skin, below which lies a seething cauldron of cholesterol-laden gunk. If this "unstable" covering ruptures, the contents will be released and a clot will form inside the artery at the location of the rupture that can block the flow of blood through the artery. Equally devastating, the clot can form and then break loose from its moorings on the inner arterial wall, travel a short distance, and lodge downstream where the vessel narrows. This causes an "infarction."

Blockage of downstream flow in the vessel unleashes the horrific cascading sequence of events we call a heart attack: oxygen deprivation in the tissues served by the vessel, chest pain, shortness of breath, collapse, resuscitation, the risk of sudden death, ambulances, emergency rooms teeming with excellent highly skilled and dedicated workers hell bent on saving another life, intravenous clot busting drugs, pain relievers (usually morphine), hospitalization, cardiologists, get-well cards. And—in about half of all cases—a funeral.

Atherosclerotic plaque itself is not so dangerous, but *unstable* plaque is. We used to think that the most dangerous plaques were the largest ones, but now we know that the older, well-established plaques—because they slow the flow of blood—are the most likely to cause angina (chest pain), but are *not* closely associated with heart attacks. It's the small new plaques that haven't yet healed over—the "unstable" ones—that cause heart attacks.

What's an ideal Cholesterol and LDL level?

A normal healthy person has no more than two grams of cholesterol per liter of plasma. We measure cholesterol in tenths of a liter (or deciliters), so that comes to a little less than 200 mg per deciliter. As the level rises above 200, so does risk. By the time serum cholesterol has reached 260 mg/dL the chances of a heart attack have risen to 500%, or five times the risk of a person with a level below 200.

A healthy LDL level is below 90 mg per deciliter. LDL rises with cholesterol, so when cholesterol is elevated, so is LDL.

Lowering Cholesterol works

No expert seriously questions the fact that lowering cholesterol slows, stops, and may even reverse plaque buildup and heart attack risk. However, experts most definitely do differ as to the best means to achieve this end. No doctor, alternative or mainstream, questions the value of severely restricting animal fat. Mainstream doctors, however, are smitten with the statin drug approach—but this has some serious drawbacks. Statin drugs routinely cause unwanted side effects such as muscle damage (statin-induced myopathy), liver damage, and statin-associated dementia. (Important brain structures are made of cholesterol and in some unfortunate individuals statin drugs interfere with proper brain cell metabolism.) These problems, though widely ignored and/or pooh-pooed by mainstream practitioners, are well-documented in the scientific literature. Ex-astronaut Duane Graveline, M.D., in his book “*Lipitor: Thief of Memory*,” recounts the horrifying story of his own statin-induced global amnesia, and elucidates the many problems caused by these drugs.

The good news is that we have natural alternatives to statins that are just as effective but don’t cause unwanted side effects and toxic reactions. Red rice yeast extract, pomegranate juice, and serrapeptase are among the many natural choices that lower cholesterol without toxicity. (See end of this chapter for all the treatment options.)

Lowering blood cholesterol (and with it, LDL) provides two distinct benefits. First, if there is less cholesterol to get trapped in plaque, overall plaque size will be smaller. Second, *lowering cholesterol increases plaque stability*—that is, it decreases the chances that unstable plaque will rupture, causing a heart attack. Even people who have already had a heart attack can substantially reduce the risk of a repeat simply by cholesterol reduction. But please: do it naturally!

Lowering your elevated cholesterol and LDL dishes out some impressive benefits. One major study followed for five years 4400 patients who had already had heart attacks. The only intervention in these patients was aggressive lowering of their cholesterol. The authors concluded that if a typical practitioner simply lowered cholesterol in his or her patients, after five years:

- Forty people would be saved out of the 90 who would otherwise die from heart disease.
- Seventy of the expected 210 nonfatal heart attacks would be avoided.
- Bypass surgery, angioplasty and stent procedures would be avoided in 60 of the 210 patients who would have otherwise needed these procedures.

Clearly, cholesterol reduction works. If we take a closer look at the same data, however, another story emerges—one that underscores lipid panel limitations and the importance of comprehensive testing. In the five years of this study, almost half of these patients had a negative outcome. For every 1000 patients:

- 140 went on to have another nonfatal heart attack
- 90 died of heart disease
- 150 went on to require a surgical procedure

Keeping Cholesterol and LDL in perspective

Overwhelming evidence tells us that LDL and cholesterol are bad actors. There is no question that if your cholesterol level exceeds 200, you need to get it down. However, our

national fixation on cholesterol has pushed aside more important markers. Millions of lives have been lost due to this costly mistake. Cholesterol and all the other markers are “independent” of one another. This means that each—without any help from the others—can cause atherosclerosis. Testing just for cholesterol (the lipid panel) just won’t cut it anymore: we need to measure and treat them all.

Why the cholesterol fixation? Why do most doctors refuse to test and treat for other, more accurate markers? One reason is that drugs provide the illusion of an easy fix. All the physician has to do is whip out his or her prescription pad and lower his patient’s cholesterol. There’s no statin, however—no quick and easy drug fix—for the remaining markers. Even though they all contribute to the disease process, only their weakest and least relevant member, cholesterol, gets addressed. No wonder so many people with normal cholesterol levels have heart attacks!

The problem comes down to cash flow. Nutritional supplements, exercise, and dietary changes don’t generate income for Big Pharma. Massive numbers of people are dying of a preventable disease, but the industry assigned to treat it is motivated by profits. Patient welfare takes a back seat. Atherosclerotic disease is preventable and reversible, but until our health care industry develops a genuine desire to address and cure the underlying causes of this epidemic, it will continue.

How to Lower Your Cholesterol and LDL

Lowering Your Cholesterol and LDL

Low carb diet

Daily exercise

Red yeast rice extract—”Nature’s statin”—Take 1-2 600 mg. capsules twice daily. Used in Chinese Traditional Medicine for over a thousand years, red yeast rice extract consists of naturally-occurring medicinal compounds that regulate lipid levels without the dangers associated with statin drugs. Used to cure heart disease and circulatory disorders since the Tang Dynasty (800 A.D.), this potent herbal lowers cholesterol, triglyceride and low-density lipoprotein (LDL) levels. Contains heart-friendly phytonutrients that go far beyond simply lowering cholesterol to provide a broad spectrum of cardiovascular benefits. Red yeast rice lowers Coenzyme Q-10, so add 50 mg. a day of **Coenzyme QH** daily.

Pomegranate juice—Drink 6-8 ounces of pure juice daily. Lowers cholesterol and LDL, reverses atherosclerosis, melts away advanced plaque while reducing LDL oxidation. Pomegranate juice is the most powerful fruit-derived antioxidant. Must be pure organic—i.e., made from whole whole fresh fruit, no other ingredients, no other juices, no additives, not from concentrate. Use Lakewood brand “Pure Pomegranate.”

Curcumin (a component of the spice turmeric)—2-8 500 mg. phytosome capsules twice daily, or use turmeric liberally in cooking. 2-8 grams a day have been used in research studies. Lowers cholesterol and LDL and reverses atherosclerosis. Stick with Meriva® “phytosome” products in which curcumin has been bonded to a fat soluble substrate (phosphatidylcholine) to enhance absorption.

Green Tea Extract—1-2 capsules twice daily. Green tea reduces cholesterol and LDL by increasing LDL receptor expression (as measured by LDL receptor binding activity) in the liver. Upregulating the LDL receptor reduces cholesterol by 30%.

Therapeutic Goals

Lower cholesterol to ideal level of 170-200 mg/dL

Lower LDL to ideal level of 70-90 mg/dL

Basic program to lower Cholesterol and LDL

The four most effective nutritional supplements for lowering cholesterol and LDL are **red yeast rice extract**, **pomegranate juice** (organic Lakewood PURE Pomegranate), **curcumin** (as Inflammation Control), and **green tea extract**. These food-derived, phytochemicals should be the starting point for your cholesterol-lowering program.

Curcumin—(2-8 500 mg capsules twice daily, or use turmeric liberally in cooking. 2-8 grams a day have been used in research studies. Though it prevents and reverses atherosclerosis via numerous mechanisms, curcumin is not well-absorbed. Purchase only “phytosome” products

in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption.

Green tea extract (1-2 capsules twice daily).

Garlic capsules (1-3 once or twice a day).

Low-carb, low-fat diet that minimizes animal foods (meat, eggs, dairy). Minimal amounts of extremely lean meat. Eat lots of veggies, beans, fruit, nuts and seeds.

Daily exercise

Red Yeast Rice Extract

Take 1-2 600 mg capsules twice daily.

Used in Chinese Traditional Medicine for over a thousand years, red yeast rice extract (Hong Qu) is the original herbal statin drug. This medicinal herb is just as effective as its modern drug knockoffs, but isn't plagued by the host of dangerous side effects that accompany the use of statin drugs.

As described in the ancient Chinese pharmacopoeia, Ben Cao Gang Mu-Dan Shi Bu Yi, published during the Ming Dynasty (1368-1644), the use of red yeast rice in China to cure heart disease and circulatory disorders was first documented in the Tang Dynasty (800 A.D.) and has been used ever since.

Red yeast rice is made by fermenting rice with *Monascus purpureus*, a type of red yeast. (Red yeast rice extract does not contain any yeast, however.) In the 1950s modern drug researchers, recognizing the potential medical importance of red yeast rice extract, but realizing they couldn't make a profit selling a non-patentable Chinese herb, stripped out the single most effective molecule (discarding the crucial supporting components), and then synthesized it. The result was the original statin drug: lovastatin (Mevacor). Unlike the Chinese herb, the synthesized drug causes severe musculoskeletal symptoms and brain damage.

Plant medicinals (herbs) contain a spectrum of active ingredients. Isolating and purifying one patentable molecule, while tossing out the other members of the family of beneficial compounds, is a prescription for side effects and toxicity. Statins are no exception. Statins, the drug version of red yeast rice extract, commonly cause severe musculoskeletal symptoms, including muscle cramping, rhabdomyolysis (breakdown of muscle tissue), myositis (inflammation in the muscle), and myalgia (pain in muscles). These symptoms are usually missed by the prescribing physician, who chalks them up to muscular misuse or old age. These adverse reactions are not seen in patients using red yeast rice extract.

The most ominous adverse reaction, however, is *statin-associated dementia*. This syndrome has been documented by several research reports in the scientific literature, and thousands of anecdotal reports. The "statin effect study," where patients on statins self-report side effects, tells us that 48% of patients on statin drugs report some degree of mental impairment. Statin-associated memory loss, difficulty concentrating, cognitive impairment, and either global or partial amnesia are the dark side of statins.

One of my patients comes to mind. Millie had been misplacing her keys, losing track of what she was doing, becoming easily confused. I told her about statin-associated dementia, and suggested she try going off her statin for a while. Within a week her brain started functioning again and all her symptoms went away. When Millie told her cardiologist what she had done, he fussed and fumed, called it balderdash and horsefeathers, and insisted she get back on her statin

drug. Millie complied, but within a week, her cognitive and memory problems had returned in full force. She quit again, this time for good.

I recommend red yeast rice extract to my patients because it very effectively lowers cholesterol, triglyceride and low-density lipoprotein (LDL) levels and provides broad spectrum cardiovascular benefits without the potential toxicity of statin drugs. Red yeast rice extract outshines statins because it contains an array of naturally-occurring heart-friendly phytochemical compounds (mevinolin, beta sitosterol, stigmasterol, isoflavones, and monounsaturated fatty acids), rather than just one purified drug molecule.

Red yeast rice extract, like statin drugs, reduces levels of coenzyme Q-10, so this must be replaced. Take 50-200 mg a day of Coenzyme QH (the more active, *reduced* form of coenzyme Q-10).

Pomegranate juice

Drink 6-8 ounces of pure organic pomegranate juice daily.

Pomegranate juice is almost too good to be true. Pomegranate doesn't just lower cholesterol; it also *reverses atherosclerosis*! And it tastes great too.

Delivering a cornucopia of phytochemical compounds, and rich in polyphenols, pomegranate has been shown to block cholesterol synthesis, melt away advanced atherosclerotic lesions in humans, reduce LDL oxidation, and prevent the accumulation of cholesterol in macrophages that leads to the formation of foam cells. This delicious, sweet ruby red juice also lowers blood pressure by inhibiting angiotensin-converting enzyme (ACE). It reverses the carotid intima-media thickening caused by atherosclerosis. It reduces platelet aggregation, rendering blood less likely to clot, thus reducing risk of thromboembolic disease.

This incredibly versatile fruit serves up potent anti-cancer (breast, prostate, colon, leukemia) and immuno-potentiating effects, and has even been shown to protect against osteoporosis.

If that weren't enough, pomegranate juice is the most powerful fruit-derived antioxidant, and has been shown to reduce oxidative stress everywhere in the body.

Any old pomegranate product won't do. The juice must be pure—no other ingredients, no other juices, and no additives. It must be made from whole fresh fruit, not from concentrate, because processing damages its sensitive phytochemicals. It must be organic. The only brand I have been able to find that fits this description is Lakewood "Pure Pomegranate." Avoid pomegranate in capsules, as processing into a powder denatures some of its more sensitive components.

Why haven't you heard about the wonders of pomegranate juice? Trust me here, if Big Pharma could profit from peddling pomegranate juice, you would have already seen TV ads promoting it as more effective than statins. The drug industry's multi-billion dollar statin market would vanish overnight if the public became aware of the power of pomegranate juice.

Curcumin

Take 2-4 caps twice a day (Inflammation Control; Renewal Research). Make sure the word "Meriva®" appears on the label.

Curcumin (curcumin longa) is the bright orange-colored active ingredient in the popular native Indonesian and South Indian spice, turmeric. Curcumin contains an array of potent antioxidant and anti-inflammatory compounds shown to block many of the molecular biological changes that can lead to stroke and heart attack. Beyond lowering cholesterol and LDL, researchers have shown that curcumin exerts the following amazing array of vascular effects:

- blocks initiation and progression of atherosclerosis
- prevents oxidation of LDL (oxidized LDL inflicts damage to the arterial wall, causing atherosclerosis)
- reverses the endothelial dysfunction caused by high glucose levels (seen in patients with insulin resistance and TMS)
- reverses the vascular dysfunction and endothelial damage caused by oxidative stress
- anti-thrombotic—that is, prevents abnormal platelet aggregation, thus reducing the probability of clot formation
- blocks overstimulation of the inflammatory response that accelerates cardiovascular disease
- inhibits proliferation of vascular smooth muscle cells, which blocks increases in arterial wall thickness associated with cardiovascular aging and arteriosclerosis.
- reduces systemic inflammation by inhibiting inflammation-stimulating transcription factor NF-kappa B, the inflammatory enzymes COX-2 and 5-LOX, and cytokines, including interleukin 6 and TNF (tumor necrosis factor).
- reduces C-reactive protein (CRP) levels
- increases HDL (HDL removes cholesterol from atherosclerotic arteries and returns it to the liver for removal. High levels of HDL protect against atherosclerosis.)
- strengthens and protects the cardiovascular system
- inhibits fat cell-derived inflammatory mediators. (Fat cells, also known as *adipocytes*, generate low grade, chronic inflammation that leads to cardiovascular disease and to insulin resistance.)
- exerts several other biological effects associated with preventing chronic disease and slowing the aging process



Curcumin

Beyond its vascular effects, curcumin displays a remarkable array of healthful, curative, even life-extending properties. Hundreds of research studies have documented curcumin's medicinal effects: anti-cancer, anti-arthritic, anti-inflammatory, anti-depressant, pain-reducing, hepatoprotective, antihypertensive, and antibiotic.

Dose and delivery: 2-8 500 mg capsules twice daily, or use turmeric liberally in cooking. 2-8 grams a day have been used in research studies. Curcumin is not well-absorbed. Purchase only "phytosome" products in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption.

Green Tea Extract (*Camilla sinensis*)

Take 1-2 capsules twice daily.

Green tea is the second most consumed beverage in the world (water is in first place). A huge amount of published research—including 25 years of clinical trials in Europe and Asia—has demonstrated that green tea delivers a phytochemical bonanza of health benefits. Rich in flavonoid catechin polyphenol antioxidants such as EGCG (epigallocatechin gallate), green tea not only protects against cardiovascular disease; it also reduces the risk of cancer, impaired immune function, osteoarthritis, infection, gum disease, and even tooth decay.

The LDL receptor (a cell-surface protein that latches onto LDL particles) is the major mechanism by which the liver removes cholesterol from the bloodstream. Low LDL receptor function is seen in individuals with elevated cholesterol. Green tea reduces cholesterol and LDL by increasing LDL receptor expression—i.e., green tea encourages increased production (via gene expression) of LDL receptors (as measured by LDL receptor binding activity, protein and mRNA)—in the liver. By up-regulating the LDL receptor, green tea reduces cholesterol by 30%.

EGCG, the main active component in green tea leaves, protects your cells from oxidative damage by those nasty omnipresent free radicals that can shorten your life by causing cancer, arteriosclerosis, heart disease and accelerated aging. EGCG inhibits oxidation of fats (including the all-important LDL particle), lowers cholesterol, and blocks the development of the clots (called anti-thrombotic activity) that lead to heart attacks and strokes.

The polyphenols in green tea improve blood sugar regulation in persons with insulin resistance.

Green tea protects the endothelium from oxidative and inflammatory damage.

Green tea has been shown to assist in weight loss.

EGCG and other green tea phenols also protect our DNA from ultraviolet and visible radiation-induced damage: at least one researcher has shown that sipping green tea before exposure decreases sunburn.

Black tea leaves contain a little EGCG but much less than the green alternative.

Garlic

Take 2-4 400 mg capsules twice daily.

Flaxseed oil

Take 4-6 1000 mg capsules daily.

One tablespoon or 6 caps daily. Essential fatty acids lower LDL and cholesterol and provide the raw material for our bodies to synthesize inflammation fighting prostaglandins. Flaxseed oil is as effective as fish oil at reversing heart disease and is preferable for several reasons, not the least of which is that it is not contaminated with mercury.

Marine Lipids (fish oil; EPA and DHA)

Take 2-4 1000 mg capsules twice daily.

In 2000 the Mayo Clinic published a review of 18 trials including 823 subjects, establishing that fish oil supplements significantly reduce triglyceride levels. (Motori VM, 2000).

According to American Heart Association's guidelines (AHA Statement 11/18/2002), people who have elevated triglycerides may need 2 to 4 grams of EPA (eicosapentanoic acid) together with DHA (docosahexanoic acid) per day provided as a supplement.

Dietary changes that will lower your Cholesterol and LDL

- **Low-fat diet**; discontinue or minimize all animal fat. Reduce or eliminate saturated (animal fat) consumption, including fish, organ meats, high-fat dairy, fried foods. Replace fat with protein and vegetables: modest amounts of lean organic chicken or turkey meat, lean beef and pork, soy protein products like breakfast links (more soy ideas below), rice protein powder, or soy protein powder. Cook with coconut oil (high in good mono-unsaturated fats, zero cholesterol). Use extra virgin olive and/or flaxseed oils (Barlean's brand) on salads or in dressings.
- **Low-cholesterol diet** (cholesterol comes only from animal products; no plant-derived food contains cholesterol)
- **Low-carbohydrate diet** (See Chapter 11 for how to do a low carb diet.)
- **Beans** (all)
- **Nuts**—All nuts (walnuts, almonds, peanuts, pistachios, cashews, pecans, Brazil nuts, etc.) contain heart healthy omega-3 oils and antioxidants. The FDA now allows label claims on nut containers for heart disease risk reduction.
- **Shiitake mushrooms**
- **Soy protein**—tofu, soy milk, soy nuts, tempeh, raw soybeans (but *not* soy sauce, soy oil, most soy burgers, soy cheeses, and soy hot dogs)
- **Artichoke and artichoke extract.** In one 6-week trial 1800 mg of artichoke extract consumed daily lowered total cholesterol by 18.5% in the treatment group versus 8.6% in the placebo group.
- **Oat bran** (not oats) lowers cholesterol and LDL. In one study, two ounces of oat bran per day caused a 16% lowering of LDL.
- **Avocados** (for their monounsaturated fat, oleic acid content)
- **Olives and olive oil**
- **Carrots**
- **Chili peppers**
- **Apples** (for their soluble fiber)
- **Blueberries** contain pterostilbene (anticancer, lowers cholesterol and triglycerides, reverses cognitive decline) and a host of other healthful phytonutrients.

Lifestyle Cholesterol and LDL lowering agents

Exercise is essential! One hour every day, divided equally into strength and cardio. All forms of exercise lower cholesterol and LDL. It is unlikely that you can lower your cholesterol and LDL levels without exercise. As an added benefit, exercise has been shown to reverse plaque.

Make sure you are not hypothyroid

A **low thyroid elevates total cholesterol and LDL**. Doctors usually miss an elevated cholesterol level when its caused by subclinical hypothyroidism. Undetected hypothyroidism is very common, especially in people over 40. You can't trust your doctor to correctly diagnose hypothyroidism. Anyone with a TSH of 2.0 or more is almost certainly hypothyroid. If your free T3 level is 3.5 or less you are hypothyroid. Take the Basal Metabolic Temperature Test (oral temperature upon arising) on your own at home as described in chapter 36 of my book, *Renewal: the Anti-Aging Revolution*. (Published by Rodale Press and St. Martin's Press). If your basal temperatures are consistently low (below 97.8), you are definitely hypothyroid. If you have symptoms of hypothyroidism and your TSH is above 2.0 (regardless of what your doctor may tell you), you are hypothyroid.

If you are hypothyroid, you will need to find an alternative/integrative doctor who can prescribe natural Armour Thyroid and do followup testing to make sure you are in thyroid balance.

Additional Cholesterol and LDL-lowering agents

- **Daily Multivitamin-Mineral**. Take the full recommended dose of a top quality multivitamin every day.
- **Alpha Lipoic Acid**—100-600 mg per day in divided doses
- **Vitamin C** (Buffered C or Ester-C)—2000-6000 mg per day
- **L-Carnitine** (1500-3000 mg/day)—Also helps weight loss. Fat can't be burned without L-Carnitine.
- **Chromium** (200-600 mcg/day)
- **Fiber (dietary and supplemental)**
- **Ginger**
- **Fenugreek**—lowers triglycerides and blood sugar.

Drugs* that lower Cholesterol and LDL

- **Niacin** (nicotinic acid). I never recommend niacin therapy to lower cholesterol or raise HDL. Niacin, though it causes flushing and toxicity, is very effective at raising HDL. Yes, niacin *is* a vitamin, but I choose to list it here as a drug because dangerously high *pharmacologic* (as opposed to low *physiologic*) doses are necessary to reduce cholesterol and raise HDL. One study showed a 33% elevation in HDL after six months of use. High dose niacin works because an overdose of this essential nutrient effectively poisons the liver's cholesterol-manufacturing mechanism. These pharmacologic doses, however, can (and do) cause liver damage—definitely *not* what Mother Nature would recommend. There are other ways to lower your cholesterol without risking liver

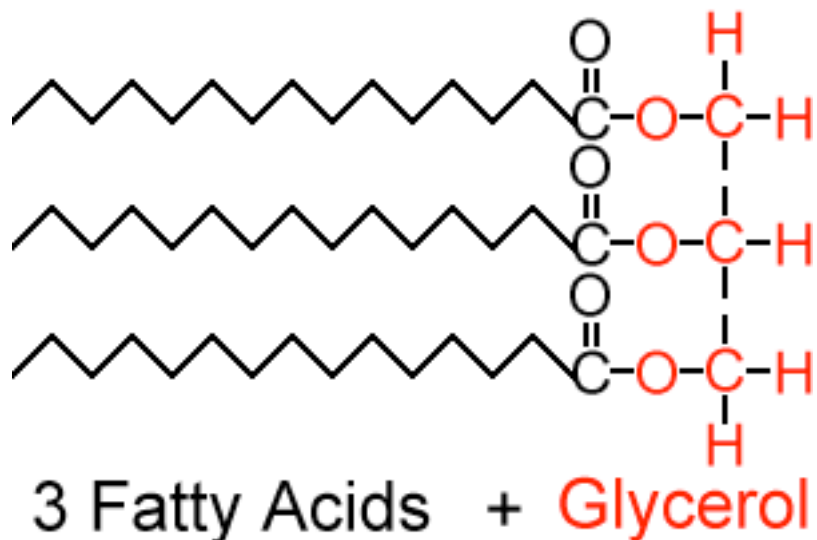
damage. If you do choose to take high-dose niacin, careful monitoring of liver enzymes is absolutely necessary. The inositol hexaniacinate form of niacin sidesteps the discomfort of flushing, but not the high pharmacologic dosing.

- Statins - not recommended unless you fail to see reductions of cholesterol and LDL after 6 months of daily therapy using red yeast rice extract and pomegranate juice.
- Bile acid sequestrants
- Fibrates

* I don't recommend taking these. They are included for informational purposes only.

Triglycerides

Your Fat Transport System



A triglyceride molecule

What is a Triglyceride?

As discussed in the section above on Lipoproteins, the body needs to make fat molecules water-soluble so it can transport them in the blood stream. Triglycerides are the answer. Here's how it works. Start with glycerol, a small molecule that loves to carry fatty acids around. Each glycerol molecule has three attachment sites—three places where it can “hold hands” with a fat molecule. When all three sites are filled, we have a *triglyceride*.

Glycerol isn't particular about who it holds hands with so long as it looks like a fatty acid: any type of fat molecule can attach to its three sites. They might be the unhealthy, pro-inflammatory saturated fatty acid molecules we find in animal products like dairy, eggs, cheese,

poultry, and red meat. They might be the really nasty *trans*-fats we find in junk, fried, and fast food—or they might be the healthier polyunsaturated oils we find in plant foods and oils. Or the glycerol could be carrying the best fats of all, the essential fatty acids like alpha linoleic acid, which we get from walnuts, olives, and flaxseed oil. Whatever kind of fat they are, they are bound, three at a time, to the glycerol “carrier” as a triglyceride for delivery to their respective job sites.

Triglycerides ride around in the bloodstream alone, but they also get packaged up into larger transport vehicles, the lipoprotein particles discussed earlier in this chapter: HDL, LDL, and VLDL. The triglyceride level that is part of a lipid panel measures only the triglycerides that are free, not those already packaged up inside of LDLs, HDLs and VLDLs.

The importance of Triglycerides

It should not surprise you that an elevated triglyceride level is very useful for predicting cardiovascular disease risk. Degree of triglyceride elevation predicts both the severity of atherosclerosis and the likelihood of a heart attack or stroke. Multiple studies have shown a near linear relationship between triglyceride concentration and coronary heart disease event rates.

Individuals with high triglycerides are also at high risk of developing insulin resistance (the metabolic syndrome (see Chapter 11)).

If your triglycerides are elevated it means there’s too much fat in your blood. Obviously, a diet high in fats will raise serum triglycerides. Even though triglycerides are fat molecules, an elevated triglyceride level doesn’t necessarily come just from the fats you have eaten; it can also be caused by eating too many carbs.

When we eat too many carbohydrate-containing foods, our body gets rid of the extra carbs—the ones we don’t burn off immediately—by packaging them up as triglycerides. So excess carbohydrate consumption causes triglyceride level elevation. Is it no wonder that research clearly shows that reducing carb intake and increasing exercise (to burn off the extra carbs) lowers triglyceride levels and protects against atherosclerosis?

Another separate, but equally serious problem caused by elevated triglycerides is impaired fibrinolysis (clot dissolving). Unless our bodies can get rid of clots rapidly, the likelihood of a stroke or a heart attack increases exponentially.

Finally, triglyceride elevations have the undesirable effect of driving down “good” HDL levels.

So we have many reasons to watch our triglycerides closely and work to keep them in the normal range. (See end of this chapter for treatment recommendations.)

How to Lower Your Triglyceride Level

Therapeutic Goal: Lower triglycerides to 150 mg/dL or less.

Lowering Your Triglyceride Level

Diet—Carbs and fats drive up triglycerides, so eat a low carbohydrate diet and reduce fat from all sources, especially beef and dairy. Eliminate sugars and refined or processed carbohydrates. Focus on high fiber foods.

Daily exercise—mixed aerobic and non-aerobic.

Nutritional medicines

- **Acetyl-L-carnitine**—one to two 500 mg. capsules once or twice daily
- **Curcumin** (a component of the spice turmeric)—2-8 500 mg. capsules twice daily, or use turmeric liberally in cooking, 2-8 grams a day. Stick with “phytosome” products in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption
- **Flaxseed oil**—one tablespoon or 6 capsules daily.
- **Fish oil capsules** (Marine Lipids)—1000 mg. 1-2 capsules twice daily.
- **Artichoke extract**—1-2 capsules daily

Basic Program for lowering Triglyceride level

Eat more fruits, vegetables, and beans.

A **low-carbohydrate diet** is essential for lowering triglycerides because excess carbohydrates drive triglyceride levels up. Eliminate all refined carbs and sugars. Small quantities of unprocessed, complex carbohydrates (beans, nuts, seeds, whole grains) are acceptable.

Eliminate sweets and all foods that contain added sugar, including juices, baked goods, processed foods, and snacks.

Low-fat diet. All dietary fats, but especially animal fats and hydrogenated oils, elevate triglyceride levels.

Acetyl-L-Carnitine (ALC) (500-1000 mg once or twice a day). Acetyl-L-Carnitine's primary role in the body is to transport fats (triglycerides) into our mitochondrial energy factories so they can be used as fuel. ALC accelerates the burning of fats by shuttling them into your heart muscle cells to be burned for energy. Without ALC, fatty acids (TGs) are unable to penetrate the membrane of the mitochondria, resulting in a decreased rate of fat utilization and energy, and a weaker heart muscle. ALC is not an amino acid; it is a vitamin-like nutrient related to the vitamin-B family. When subjects with hypertriglyceridemia (elevated triglycerides) were given 900 mg per day of supplemental ALC, blood triglycerides plummeted from an initial value of 440 mg/dL to 186 mg/dL after eight weeks of treatment. ALC also lowers cholesterol and improves cognitive functioning.

Flaxseed oil (1 tablespoon or 6 capsules daily).

Marine lipids (3-5 1000 mg capsules daily). In hundreds of studies DHA and EPA in this dose range have consistently shown triglyceride-lowering properties. A 2000 Mayo Clinic review of 18 trials including 823 subjects established that fish oils significantly reduced triglyceride levels. In 2002 the American Heart Association's guidelines for people with elevated triglycerides included a recommendation to take 2-4 grams daily of the two main components of marine lipids: EPA (eicosapentanoic acid) and DHA (docosahexanoic acid).

Garlic and onions or garlic extract capsules (2-4 twice a day).

Additional nutritional medicines that lower Triglycerides

Curcumin—1-8 grams a day of turmeric or 4-8 capsules a day of Inflammation Control (Renewal Research). See description of curcumin in "Basic program to lower Cholesterol and LDL" above.

Multivitamin—Renewal Research (or another top quality multi) daily; take amount recommended on label.

Cinnamon extract (Cinnulin®)—A study reported in *Diabetes Care* showed that after 40 days of treatment with Cinnulin® cinnamon extract, triglyceride levels in 60 patients had dropped 23-30% as compared with controls given a placebo.

Artichoke extract—Several studies have shown that artichoke blocks cholesterol production in the liver and lowers triglyceride levels.

Chromium (200-1000 mcg daily).

Daily Fiber.

These dietary changes will lower your Triglycerides

- **Low-carbohydrate diet.** Restrict carbohydrates! Excess carbohydrates drive triglyceride levels up. A low carbohydrate diet is essential for lowering triglycerides. Eliminate refined carbs and sugars. See Chapter 11 for information about low carb dieting.
- **Low-fat, low-cholesterol diet.** Animal (saturated) fats and hydrogenated oils elevate triglyceride levels.
- **Pomegranate juice** (pure organic Lakewood Pure Pomegranate)
- Eat plenty of **fruit and vegetables.**
- **Blueberries** contain pterostilbene (anticancer, lowers cholesterol and triglycerides, reverses cognitive decline, protects against macular degeneration) and a host of other healthful phytochemicals.
- **Minimize alcohol** (high sugar content).
- **High-fiber diet** (supplement with Daily Fiber from Renewal Research).
- **Reduce or eliminate saturated (animal fat) consumption.** Eliminate fish and other fatty meats; substitute with small quantities of lean free-range, humanely raised chicken or pork. Replace animal protein with soy products like tofu, soy burgers, and breakfast links. Use rice protein powder.

Lifestyle changes that lower Triglycerides

Exercise is very important! One hour daily, cardio and strength. All forms of exercise lower triglyceride levels. Get used to this idea: the triglyceride research literature strongly suggests that it is unlikely you'll be able to lower your triglyceride level without daily exercise.

Modest Weight loss (10-15 lbs.) can greatly reduce your triglycerides.

Correct subclinical hypothyroidism

Make sure you are not hypothyroid. Undetected hypothyroidism is very common and causes triglycerides to go up. Take the Basal Metabolic Temperature Test on your own at home as described in chapter 36 of my book, *Renewal: the Anti-Aging Revolution* (published by Rodale Press and St. Martin's Press). If your basal temperatures are low (below 97.8), you are hypothyroid. If you have symptoms of hypothyroidism and your TSH is above 2.0 (regardless of what your doctor may tell you), you are hypothyroid. If your free T3 level is below 3.5 pg/ml, you are hypothyroid.

Factors that cause Triglycerides to go up

- **Insulin resistance and the metabolic syndrome** (syndrome X); see Chapter 11
- Uncontrolled **adult onset (type II) diabetes**
- Undetected **hypothyroidism.** Take the Basal Metabolic Temperature Test on your own at home as described in chapter 36 of my book: *Renewal: the Anti-Aging Revolution.*)
- **Alcohol** consumption
- **Insufficient Omega-3/6 fatty acid** consumption
- **Weight gain**
- **High-carbohydrate diet**

- **High-fat diet**
- **Oral estrogen containing contraceptives**
- **Corticosteroid drugs**
- **Hepatic and renal disease**

Drugs* that lower Triglycerides

- Statins
- Gemfibrazil
- Probucol
- Fibrates
- High-dose niacin

* I don't recommend taking these. They are included for informational purposes only.

HDL

“Good” Cholesterol

What are HDL particles and what do they do?

High-density lipoproteins (HDLs), the smallest lipoprotein particles, are about one-third the size of LDLs and carry about one-third of all the blood cholesterol. In the submicroscopic nanoscale world of lipoprotein particles, HDL is the veritable “good guy,” the hero who specializes in protecting us from the nasty LDLs that cause atherosclerotic plaque.

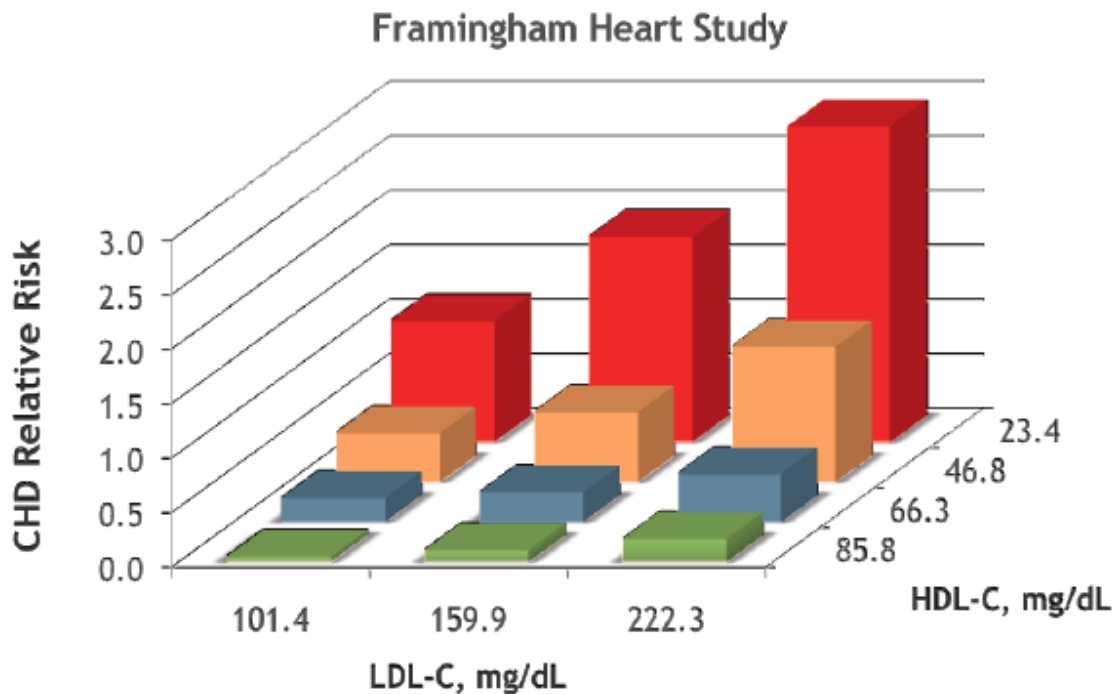
Like LDL, HDL is made in the liver, and plays a very important role in cholesterol metabolism: HDL finds and latches onto cholesterol molecules, and then escorts them back to the liver so they can be booted out of the body. We call this “reverse cholesterol transport.”

HDL is kind of like the sheriff: its sole mission is to ride out and nab excess cholesterol molecules, handcuff them, and then deliver them to the liver, which then expels them from the body. By taking up the extra cholesterol, HDL prevents LDL from grabbing it. That's one reason (of several) why HDL is famous for reducing the risk of atherosclerosis. Though HDLs are known as “good cholesterol,” the cholesterol molecules they carry are identical to the cholesterol in LDL (so-called “bad cholesterol”) particles. HDL's ability to remove extra cholesterol and dispose of it is what makes it “good.”

HDL particles go beyond merely removing excess cholesterol from the bloodstream; they also possess the unique capacity to remove cholesterol that has already been deposited in atherosclerotic plaque.

Because HDL particles offer powerful protection from heart and vascular disease, you want more of them. You don't need many more, however, because small changes in HDL translate into big changes in risk: each increase of 1.0 in the HDL number (measured in mg/dL), corresponds to a 3-4% reduction in coronary heart disease risk. So, for example, a five point increase lowers risk by up to 20%.

Low HDL levels are commonly found in people who are sedentary, smoke, are overweight, have insulin resistance (see Chapter 11), have elevated triglycerides, or have chronic inflammatory disorders (see Chapters 10 on fibrinogen and 8 on C-reactive protein).



Adapted from Kannel WB Am J Cardiol. 1987; 59:80A-90A

Low HDL levels dramatically increase coronary heart disease risk.

Why is a high HDL level so important?

Individuals with higher HDL levels (>40) have much lower rates of cardiovascular disease, while those with low HDL (<40) have increased rates.

Low HDL cholesterol is a major, common, independent risk factor for coronary heart disease (CHD) and ischemic stroke, and this risk is present even when total cholesterol levels are normal.

Low HDL cholesterol is often associated with high triglyceride levels. Anything that causes high triglycerides will usually also lower HDL, and conversely, if triglyceride levels are high, lowering them raises HDL.

The most recent report of the *National Cholesterol Education Program* identified low HDL cholesterol as an independent coronary artery disease risk factor and recommended that "all healthy adults be screened for both total cholesterol and HDL cholesterol levels."

Recent landmark clinical studies have demonstrated diminished mortality and first coronary events following elevation of (a previously) low HDL cholesterol level. The *Framingham Heart Study* (a famous long-term atherosclerosis research study) produced compelling evidence that a low level of HDL cholesterol was an independent "predictor" of coronary artery disease.

For all of the markers I discuss in this book except HDL, lower levels are better. HDL is the one exception: *more* is better. An ideal HDL level is at least 40, preferably in the 50s, and the lowest possible risk is at 60 or more. If your HDL is low (i.e., below 40), use the information at the end of this chapter to design and implement a personal program that will raise it up to healthy levels.

HDL protects against atherosclerosis by depriving macrophages of their lunch

When oxidized LDL particles find their way into your arterial wall (see chapter 5 on Atherogenesis), monocytes (small white blood cells) follow them in. Once inside the arterial wall, these monocytes morph into much larger cells called macrophages, which then proceed to gobble up (we call this phagocytosis) LDL particles and the cholesterol they contain. These fat-engorged macrophages grow to an enormous size, too big to get back out of the arterial wall, so they become trapped there and die. The buildup of cholesterol and debris from dead macrophages causes plaque.

HDL particles abort the above-described process, thus thwarting atherosclerotic plaque formation. HDL literally snatches extra cholesterol molecules away from the jaws of the macrophages about to devour them. Then HDL then gently ushers the cholesterol back into the bloodstream, and then to your liver, which expels it from your body.

Some recent research revelations about HDL

Beyond retrieving cholesterol from atherosclerotic plaque deposits and taking it back to the liver, HDL particles demonstrate other properties that may contribute to its ability to protect us from atherosclerosis. HDL particles carry many lipid and protein species, several of which are biologically very active despite very low concentrations. These compounds exert influences that block and reverse atherosclerosis: they inhibit oxidation, decrease inflammation, activate the endothelium, reduce platelet activation, and control coagulation.

How to Boost Your HDL Level

Therapeutic Goal

Raise HDL to at least 40. Ideal level is 50 or more.

Raising your HDL Level

Acetyl-L-carnitine—1-2 500 mg. capsules once or twice daily

Curcumin (a component of the spice turmeric)—2-8 500 mg. phytosome capsules twice daily, or use turmeric liberally in cooking, 2-8 grams a day. Stick with “phytosome” products in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption.

Flaxseed oil—one tablespoon or 6 capsules daily. **Fish oil capsules** (Marine Lipids)—1000 mg. 1-2 capsules twice daily.

Daily exercise.

Low fat, low cholesterol, low carb diet.

Minimize or eliminate animal fat.

Eat lots of vegetables, garlic, onions, and beans (all types).

Recommended program for raising HDL

Aerobic Exercise. This can be done in many ways. Examples are jogging or fast walking one hour a day. Your heart rate will tell you whether you are in the aerobic range or not.

Low cholesterol diet. Animal foods (all meat and dairy, eggs) contain cholesterol; plant-derived foods do not.

Curcumin is a component of the Indian spice turmeric. (E.g. Inflammation Control, Renewal Research, 2-4 capsules twice a day.)

Acetyl-L-Carnitine (ALC)—By facilitating the intracellular cellular processing of fats, ALC pushes HDL upward. (500-2000 mg a day) Also supports brain health and cognitive function.

A top quality daily **multivitamin-mineral**.

Fish oil capsules (1000-4000 mg a day; Marine Lipids, Renewal Research).

Flaxseed oil (one tablespoon or 6 capsules daily).

Garlic, either dietary or as a daily supplement (2-4 capsules twice a day).

Diet to raise HDL

- **Low fat diet.**
- **Low cholesterol diet.**
- Discontinue or **minimize animal fats**. Excess consumption of animal fats lowers HDL.
- Eat **garlic, onions, shallots**. Onions (half a raw onion/day) may raise HDL as much as 30%.
- **Beans** (pintos, kidney, black, navy, lentils, chickpeas), one cup/day, will gradually raise HDL as much as 9%.
- **Olive oil** raises HDL.
- **Soybeans** (soy milk, tofu, soy nuts, tempeh, raw soybeans—but not soy sauce, soy oil, or most soy burgers, soy cheeses, or soy hotdogs) are as potent as other beans at raising HDL.
- **Oat bran** lowers cholesterol and LDL and raises HDL. In one study, two ounces of oat bran per day was associated with a 16% lowering of LDL and, after 3 months, an increase in HDL of as much as 15% (*JAMA*. 1991. 285. 1833-1839).
- **Fish oils** do raise HDL, but fish and shellfish are not acceptable sources, as *all* seafood is contaminated with mercury. Methylmercury is evenly distributed in the oceans, so shrimp, lobster, crabs, mussels, calamari, and clams have it too—even, alas, salmon. If you doubt this is true, here's my challenge: eat any combination of seafood, averaging two servings a week for three months, and then do a hair analysis for toxic minerals (you can use Doctor's Data at 1-800-323-2784). You'll see what I mean. Fish oils that have been certified mercury-free are acceptable.

Lifestyle changes that raise HDL

- **Daily aerobic exercise**-e.g., jogging or fast walking one hour a day.
- **Weight loss** and loss of body fat; leaner bodies have higher HDL levels.
- **Smoking cessation.**

Additional supplements that increase HDL

- **Chromium** (400-1000 mcg/day)
- **Magnesium** (400-1000 mg/day) (Magnesium may cause loose stools in some individuals.)

Drugs* That Raise HDL

- Statins
- Niacin (nicotinic acid). I choose to list niacin here as a drug. Niacin *is* technically a vitamin, but the pharmacologic doses required to raise HDL (and lower cholesterol) can cause liver damage, so careful monitoring of liver enzymes is required if you choose niacin therapy. Niacin, though it causes flushing and toxicity, is very effective at raising HDL. One study showed a 33% elevation after six months of use. You can try using the inositol hexaniacinate form of niacin to prevent the discomfort of flushing. But you'd still need to check liver enzymes every three months.
- Fibrates (if triglycerides are high).

* I don't recommend taking these; they are included for informational purposes only.

VLDL

Very Low Density Lipoprotein (VLDL) is type of lipoprotein particle that is structurally identical to LDL, but much bulkier. Assembled in the liver from cholesterol, triglycerides, and special proteins, the largest VLDL particles have a diameter of 30-80 nm.

Because of their size, VLDL particles contain a particularly high proportion of lipid in the form of triglyceride molecules. As VLDLs circulate through the bloodstream, their size decreases as they gradually release triglyceride molecules (which are burned off by fat and muscle tissue). Thus they gradually shrink to become low density lipoprotein (LDL) particles.

Too many VLDLs are worrisome for all the same reasons we worry about excess LDL. Elevated VLDL levels accelerate atherosclerosis and an elevation is closely associated with vascular disease in the heart, brain, and elsewhere.

VLDL may also be elevated in other diseases and metabolic states that involve inappropriate processing of lipids. The one most important to readers of this book is the metabolic syndrome, which is the subject of Chapter 10.

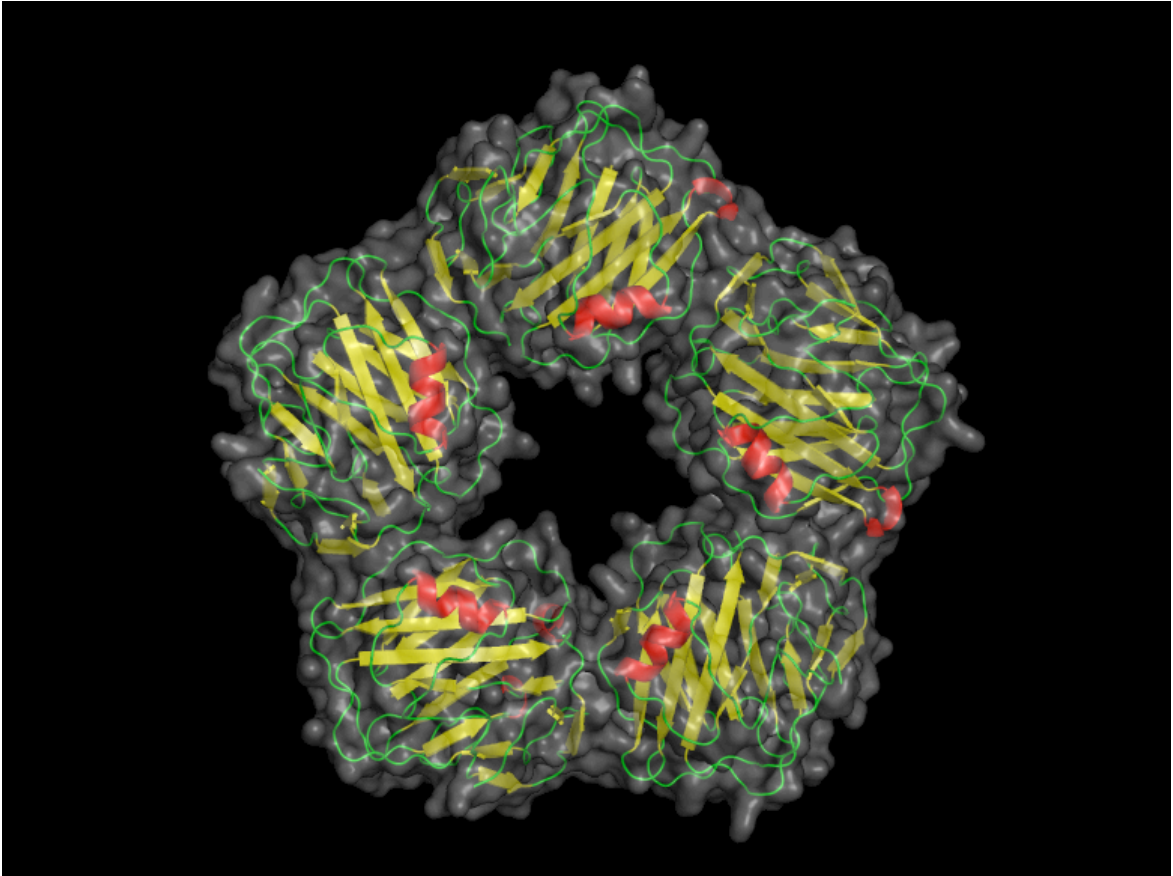
Normal range is <40 mg/dL.

How to Lower Your VLDL Level

Therapeutic goal:

Lower your VLDL to below 40 mg/dL.

VLDL levels go up and down in tandem with LDL and cholesterol. Therefore, the methods listed above for lowering cholesterol and LDL will be equally effective at lowering your elevated VLDL.



The C-reactive protein molecule.

Chapter 8

C-Reactive Protein

The fire alarm molecule

Clutching his chest, laboring to breathe, and sweating profusely, Woody Swanson pulls aside the oxygen mask, looks up at the doctor, and gasps, “What’s happening to me?” as the

paramedics unload his gurney from the ambulance and catapult it through the extra-wide doors of the Palm Gardens Hospital Emergency Room.

“Why, you’re having a heart attack, Mr. Swanson.”

“Are you sure, doc? My cholesterol is normal.”

“No time to answer that now, but I’ll tell you one thing: you’re lucky to be alive!”

Fast forward two weeks: Referred to me by a mutual friend, Woody’s first question in my office is exactly the same: “Why me, doc? My cholesterol is normal.”

“That’s true, Woody, it is normal, but cholesterol is just one marker for heart disease, and not a great one at that. Has your C-Reactive Protein ever been checked?”

“I don’t think so.”

“How about homocysteine or fibrinogen?”

“I doubt it. My doctor always just tested my cholesterol, and it has always been normal, so he always says I am not at risk of a heart attack.”

I hope he didn’t notice me rolling my eyes. “Let’s get you tested.”

A couple of days later we sit down with the results.

“Woody, now that we have a picture of your biochemical landscape, we can answer your question about why you had a myocardial infarction.”

“Well, tell me.”

“Your CRP is quite high.”

“But my cholesterol was low.”

“If your cholesterol is low, you may think your risk of having a heart attack is pretty low, but the fact is that a normal cholesterol only lowers your heart attack risk by about 30%. In fact, more than half of all heart attacks occur in people with normal cholesterol levels.”

“I guess I’m in that half, huh?”

“That would appear to be the case.”

“There should be a better way to predict heart attacks, doc.”

“There is, Woody, but most doctors don’t use it yet.”

“That is unfortunate. You guys should be finding and treating and even preventing this disease.”

“Amen. Two in three of us die prematurely of atherosclerotic disease. We do need to be more aggressive.”

“So what is this ‘better way?’”

“We could prevent almost every single heart attack if family doctors and internists included five additional markers for cardiovascular disease—homocysteine, C-reactive protein, fibrinogen, fasting glucose, and LDL Particle Size—along with their cholesterol as an annual exam.”

“Wow! It’s amazing that most doctors don’t do this. Are they pricey?”

“Not really, these tests are actually pretty inexpensive. Especially when you consider the cost of a heart attack.”

“So why don’t docs do them?”

“I don’t know, Woody. These tests are readily available and the research literature on them is quite clear: taken together, they are remarkably accurate at predicting heart attacks. And these tests are not indirect markers or “innocent bystanders”—they represent the real root causes of heart disease. The CRP, for example—the marker that apparently caused your heart attack—has been shown to be three times as accurate as cholesterol.”

“If I were a doctor, I’d test everybody.”

“Problem is, Woody, the conventional medical establishment is somewhat schizophrenic on the subject of CRP testing. For example, the American Heart Association and Centers for Disease Control recently convened a panel of experts to study this question (published in the January 28, 2003 issue of Circulation: The Journal of the American Heart Association). The doctors summarized their conclusions as follows:

- *There is “no need for CRP screening of the entire adult population as a public health measure.”*
- *“CRP can, however, be an independent marker of risk and may be useful as a discretionary tool for evaluating people with moderate risk.”*

“So they acknowledge CRP is a risk factor, but see no need to test for it, except in people of ‘moderate risk.’”

“Doc, if atherosclerosis is going to kill two-thirds of us, aren’t we all at ‘moderate risk’? Wait a minute. Aren’t we all at high risk? Shouldn’t we all be tested?”

“Yes, of course! Their dilemma is obvious, isn’t it? Pardon my cynicism, but they can’t patent curcumin, red yeast rice extract, or vitamins E and C, so there’s no profit in it. Why distract attention from the cholesterol-statin cash cow?”

“Point well taken, doc. You’d think identifying high risk patients and saving millions of lives would motivate them. I expected more. It’s a real disappointment.”

“Woody, I think many physicians are reluctant to order a CRP because they really aren’t sure what to do if they see an abnormal result. It’s one thing to tell a patient they are at great risk, but if the doctor can’t give good advice about how to correct the situation, then he or she will be reluctant to do the test.

“A 2008 New England Journal of Medicine study named JUPITER (Justification for the Use of Statins in Prevention) received a big dose of media attention because it appeared to support the idea that statins could lower C-reactive protein and thus prevent heart attacks. Finally doctors had a prescription they to write. After the initial excitement died down, however, analysts took a closer look and found deep flaws. The statin benefit was marginal at best: you’d have to give expensive statins to 200 people for a year to prevent just one heart attack. Conflicts of interest further weakened the study’s credibility: the lead researcher owned a patent on CRP testing and the drug company that funded the project peddled statins.”

What is CRP?

“So what the heck is a CRP, doc?”

“Well, technically, like cholesterol and LDL, CRP is a biochemical marker for atherosclerosis. Problem is, cholesterol’s really not a very good marker. If your cholesterol is low, you may think your risk of having a heart attack is low, but half of all heart attacks occur in people, like you, whose normal cholesterol levels have lulled them and their doctor into a false sense of security.”

“What about people with elevated cholesterol? Do they all get heart attacks?”

“No. Most people with elevated cholesterol never have a heart attack.”

“But until recently, cholesterol was all you had, right?”

“Right. We knew it wasn’t perfect, to say the least. But over the past decade we’ve developed newer better tests, tests that look directly at the various causes of atherosclerosis and heart attack. These “independent markers,” one of which is CRP, dramatically improve our predictive powers. So if we couple cholesterol with these new blood test markers, we can provide our patients with a much more precise risk assessment. The beauty of these markers goes far beyond just better testing and predicting, however.”

“How so?” asks Woody.

“Simply put, as with cholesterol, fixing the marker removes the risk created by that marker. Each of the six markers (I discuss in this book) drives a pathological process that causes arterial disease. When we correct the abnormal markers we are curing or reversing or preventing the disease process associated with that marker. Bringing each marker back to normal lowers that person’s risk (for that marker and only that marker) back to zero! And we can do it naturally, with herbs and vitamins and nutritional supplements that improve general health, rather than drugs, which, as you know, can be toxic.”

“That’s great. Wish I could have benefitted from all that information before I had a heart attack!”

“You still can, Woody! It’s true that it would have been preferable if we had found your elevated CRP before you had that heart attack, because correcting the abnormal marker (assuming no other markers were elevated) would probably have averted the event. Researchers have found that an elevated CRP more accurately predicts heart disease in men and women like you whose cholesterol and LDL levels are in the normal range. Once we get your CRP marker back to normal, your risk goes down to what it would have been if it hadn’t ever been elevated.”

“Believe me, after what I’ve gone through this past week, I’m ready, Doctor Tim. But you haven’t really answered my question. I get it that CRP is a ‘risk factor,’ but what does it do in my body? What’s the actual connection, the smoking gun, the cause and effect?”

“In a word,” I said, “it’s inflammation. Researchers now agree that inflammation is the most important single factor causing atherosclerotic hardening of the arteries. CRP is our single best marker for measuring inflammation. Known as an “acute phase” protein, CRP is the “fire alarm molecule” that alerts the entire body to injury, infection, and allergic reactions. It’s our response to any and all inflammation. The more inflammation, the higher the CRP. But CRP also causes atherosclerosis, so the higher the CRP, the more atherosclerosis. A persistently high CRP, regardless of cause, indicates a state of systemic inflammation that damages the entire vascular system.”

“So you would want to make sure your patients have a low CRP no matter what, right?”

“Right, Woody. It translates into optimum health on a multiplicity of levels.

“How does this inflammation damage arteries and lead to heart attacks and strokes?”

“Inflammation damages the endothelium, that single thin layer of cells that coats the insides of our arteries, and acts as a protective barrier to protect the rest of the artery. Once the endothelium is damaged, the barrier is breached and the nasty sequence leading to plaque formation (see Chapter 5 for details) is off and running. And inflammation also encourages coagulation, the formation of those blood clots that trigger a heart attack or stroke. Inflammation weakens the plaque deposits in atherosclerotic arteries, increasing the probability of rupture, hemorrhage, and thrombotic disease.

“I must have had a great deal of inflammation,” says Woody, “but it wasn’t showing up in the cholesterol levels my doc was ordering.”

“Exactly! Cholesterol is not a measure of inflammation. CRP is.”

“What causes the inflammation?”

Common causes of inflammation

- Weak adrenal glands (the adrenal glands make cortisol, our natural anti-inflammatory hormone; a deficiency of cortisol increases allergic, traumatic, infectious and autoimmune inflammatory reactions.
- Low grade chronic infections (a common example is periodontal infections)
- Chronic noninfectious inflammatory reactions (such as autoimmune disease and allergies)
- Free radical overload or antioxidant deficiency
- Improper diet with deficiency of antioxidant nutrients
- Elevated homocysteine levels
- Elevated fibrinogen levels
- Elevated C-reactive protein levels
- A sedentary lifestyle

“Another great question, Woody! Difficult to answer, however, because there are so many possible causes. Inflammation is the body's natural reaction to injury, allergy, or infection. Inflammation is obvious when it's on the outside—like the angry red swelling you see around a skin wound. When inflammation is on the inside—as with injured blood vessels—it's silent and invisible: we can't feel or see it. CRP is a biochemical way for us to be able to “see” the inflammation that would otherwise be invisible.”

“So when something is causing inflammation inside of me, it is also driving up my CRP and causing atherosclerosis?”

“You got it, Woody. The three go together. Anything that can cause low grade chronic inflammation has the potential to cause both arterial damage and an elevated CRP. There's another twist: CRP is not just a marker; it's also an irritant. So once CRP is elevated, regardless of cause, its very presence adds to the fires of inflammation.”

“If I get your drift, doc, you are saying that the trauma or toxin or infection—whatever it is—first causes irritation and inflammation which raises the CRP, and then both the original factor and the high CRP start working in cahoots to accelerate the atherosclerosis?”

“Yes.”

“I'd call that a triple whammy.”

Smoking gun or innocent bystander?

“Does the elevated C-reactive protein molecule contribute to the damage that causes atherosclerosis, or is it just ‘along for the ride,’ so to speak?”

“Another great question, Woody! When CRP's predictive powers were first discovered, the answer to that question was not clear. We did know that it was a large protein molecule produced in the liver as one of the body's responses to inflammation, and we did know that endothelial damage (damage to the inner lining of the artery) is the first step in atherogenesis, the arterial hardening process. For several years it was unclear whether the CRP molecule itself was adding to the arterial damage. Researchers linked an elevated CRP to several conditions that coexist with atherosclerosis. They showed that CRP elevations are seen with insulin resistance, obesity, and prior infection with three specific infectious microorganisms (all of which have been linked

to subsequent heart disease: *Chlamydia pneumoniae*, *Helicobacter pylori*, and cytomegalovirus). We also knew that CRP triggers the release of pro-inflammatory chemicals that trigger an inflammatory reaction (cytokines). So there were quite a few connections, but..."

"No smoking gun?"

"Not until 2002, Woody, when researchers at the University of California, Davis Medical Center finally showed that C-reactive protein really does damage the endothelial lining, the first step in the sequence that leads to plaque formation. Earlier experiments by researchers at the University of Texas Health Sciences Center showed that CRP acts directly on the endothelial cells that make up the inner lining of blood vessels, making them stickier (we call this vascular adhesion), so that white blood cells and inflammatory molecules are more likely to attach themselves to the endothelial surface and start forming plaque. Other scientists have shown that CRP encourages macrophages to gobble up more LDL particles, which further accelerates plaque formation.

"So" I continued, "CRP truly is a bad guy, not just a hapless onlooker. Getting rid of it—lowering ones level—is a very good idea. This is an important breakthrough because doctors (and the insurance companies that often influence diagnostic decisions) deny coverage for CRP testing, arguing that a CRP elevation doesn't zero in on the heart and that it is just a general measure of inflammation somewhere—could be anywhere—in the body. The status of CRP has now shifted from "innocent bystander" to "causative agent." The recent research has proven that an elevated CRP damages the heart regardless of where it is coming from. Thus we need to test for it routinely, and when it is elevated, we can treat the inflammatory reaction generally with nutritional medicines and lifestyle measures (see CRP lowering program at end of this chapter). When possible, we also need to find and treat specific infectious, allergic, and/or toxic causes."

"This is all so logical and straightforward that I can't believe doctors don't routinely order a CRP. I have to ask you again: why is that?"

"Physicians are reluctant to check the CRP because if a patient's level is elevated they need to prescribe a treatment for it, but no drug lowers CRP. These docs are usually unaware that nutritional medicines and lifestyle (diet and exercise) are extremely effective agents. Mainstream doctors have been so conditioned by the pharmaceutical industry to look for a drug for every problem that when confronted with an elevated lab value and nothing to write a prescription for, they feel helpless. They don't like this feeling, and can avoid it by simply refusing to order the test."

"I'm glad that isn't my problem."

"Yes, Woody, but it is very real for the millions of Americans who have HMOs, and need the doctor to write the order so that the test will be covered by their insurance."

"I get it that CRP is obviously better than cholesterol at predicting heart attacks. How much better is it?"

"Many researchers believe it is two or three times as good, but remember, cholesterol and CRP are different and additive. By which I mean that if you have an elevated cholesterol, you need to bring it down regardless of whether the CRP is elevated. Same is true of CRP: if it is elevated, you need to lower it, regardless of the status of cholesterol. Either can cause a heart attack.

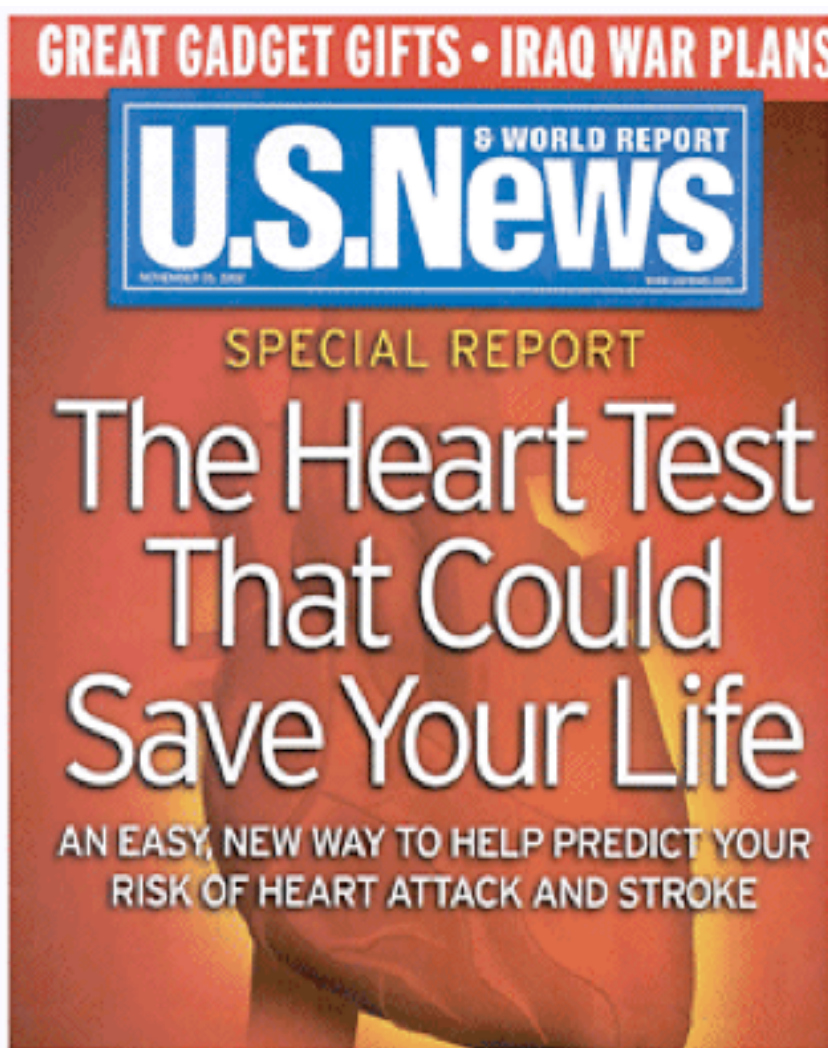
"A leading CRP researcher, Dr. Paul Ridker of Boston's Brigham and Women's Hospital, estimates that between 25 to 35 million healthy middle-aged Americans are just like you, Woody—they have normal cholesterol but above-average CRP's, putting them at unusually high risk of heart attacks and strokes. A recent study published in the *New England Journal of Medicine*

found that men whose CRP was in the top 25% had three times the incidence of heart attack and twice the frequency of stroke.”

“Doc,” says Woody, “it boggles my mind that this resource is available and most doctors don’t use it.”

“Yes, mine too. Dr. Ridker went on to add that, by testing for CRP, ‘We could prevent many heart attacks, stroke, bypass surgeries, angioplasties and save a lot of lives. To me that’s a good thing.’

“The research evidence very clearly supports the importance of CRP testing,” I continued. “Even so, in medicine, there is often a lag time between the appearance of new data and its acceptance by the medical community. I encourage all physicians to make CRP testing (and the other new markers I discuss in this book) a routine part of their regular blood testing profile. Many lives could be saved if they got on the bandwagon sooner, rather than later. At the very least a CRP, homocysteine, and fibrinogen should be done along with the usual fasting glucose and lipid panel. There is an epidemic of cardiovascular disease out there and we doctors need to start taking responsibility for finding it.”



C-reactive protein makes the cover of U.S. News on November 25, 2002

What is a normal CRP?

Risk starts at 0.56 mg/dL, and significant risk begins at about 0.8. In the 22,000 man Physicians' Health Study, CRP scores were divided into four quartiles:

- The lowest quartile had CRP levels below 0.56 mg/dL. This group had a 'relative risk' of 1.0, which means no increased risk of heart attack.
- The second quartile had higher CRP scores, between 0.56 and 1.14 mg/L. This group had a relative risk of about 1.6, meaning they were 1.6 times as likely to have a heart attack or stroke as the lowest risk group.
- The third quartile had scores from 1.15 to 2.10 mg/L for a relative risk of about 2.6, which means they were more than two and a half times as likely to have a heart attack as the group with no CRP elevation.
- The highest quartile had scores greater than 2.11 mg/L, which meant that they were almost three times as likely to have a myocardial infarction.

A CRP level like Woody's (3.8 mg/dL) put him at more than four times baseline risk of future stroke or heart attack than if his CRP had been normal, i.e., below 0.8.

So, when people ask me what is the normal range, I say the lower the better, but shoot for a level that is at or below 0.8 mg/L. Between 1.0 and 2.0 there is significantly increased risk, and above 2.0 risk is high. Ideal would be 0.56 or less."

To be sure your CRP-lowering program is working, repeat the CRP (along with any other markers that were abnormal) after two months. If you are moving in the right direction—even though you may not have yet reached your goal—stay on your program. (Remember, it may take 6-12 months or more to lower your CRP to normal, so at two months we are just looking for a trend in the right direction.) If, on the other hand, you don't see (at least) modest lowering of your CRP at two months, you will need take another look at the program options and make appropriate alterations.

How to Lower Your Elevated C-Reactive Protein

Therapeutic Goal:

Lower your CRP to the ideal level of 0.8 mg/dL or less.

Lowering Your C-Reactive Protein Level

Low carb diet

Daily exercise

Red yeast rice extract—one to two 600 mg. capsules twice daily

Coenzyme QH—one to two 50 mg. capsules daily

A daily high quality Multivitamin-mineral

Curcumin (a component of the spice turmeric)—2-8 500 mg. phytosome capsules twice daily, or use turmeric liberally in cooking

Fish oil—one to two 1000 mg capsules once or twice daily

Flaxseed oil—4-6 1000 mg capsules daily or one tablespoon of liquid (Barlean's brand recommended)

Vitamin E (as "mixed tocopherols")— one to three 400 IU capsules daily

Phytonutrient Complex—one or two capsules twice daily

Recommended program to lower your C-reactive protein

Curcumin

The active ingredient in the spice, turmeric, curcumin lowers CRP. Preferable products combine generous amounts of curcumin with other anti-inflammatory herbs such as rosemary, holy basil, barberry root, green tea, ginger, Chinese goldenthread, skullcap, and Protokin. Make sure your curcumin product contains the research-proven proprietary complex of curcumin with soy phosphatidylcholine (Meriva®). (Inflammation Control, Renewal Research; 1-4 capsules twice daily.)

Red yeast rice extract

Red yeast rice extract—the original Chinese herb from which statin drugs were purified—provides a natural alternative to statin drugs that sidesteps toxicity by retaining the natural spectrum of ingredients. (For more about statins, see Chapter 7: Lipoproteins and The Lipid Panel.)

Even though red yeast rice extract has “yeast” in its name, it does not contain yeast or any fungus.

Used in Chinese Traditional Medicine for over a thousand years, red yeast rice extract (Hong Qu) is the original herbal statin drug. This medicinal herb is just as effective as its modern drug knockoffs, but isn't plagued by the host of dangerous side effects that accompany the use of statin drugs. Because it is a food and not a drug, red yeast rice extract displays none of the harsh, toxic effects of statin drugs.

As described in the ancient Chinese pharmacopoeia, Ben Cao Gang Mu-Dan Shi Bu Yi, published during the Ming Dynasty (1368-1644), the use of red yeast rice in China to cure heart disease and circulatory disorders was first documented in the Tang Dynasty (800 A.D.) and has been used ever since.

Red yeast rice is made by fermenting rice with *Monascus purpureus*, a type of red yeast (it does not contain yeast, however). In the 1950s modern drug researchers, recognizing the potential medical importance of red yeast rice extract, but realizing they couldn't make a profit selling a non-patentable Chinese herb, stripped out the single most effective molecule (discarding the crucial supporting components), and then synthesized it. The result was the original statin drug: lovastatin (Mevacor). Unlike the Chinese herb, the synthesized drug causes severe musculoskeletal symptoms and brain damage.

Plant medicinals (herbs) contain a spectrum of active ingredients. Isolating and purifying one patentable molecule, while tossing out the rest of the family of beneficial compounds causes the widespread and well-documented side effects and toxicity that drug medicines are famous for. Statins are no exception. Statins, the drug version of red yeast rice extract, commonly cause severe musculoskeletal symptoms including muscle cramping, rhabdomyolysis (breakdown of muscle tissue), myositis (inflammation in the muscle), and myalgia (pain in muscles). These

symptoms are usually missed by the prescribing physician, who chalks them up to muscular misuse or old age. These adverse reactions are not seen in patients using red yeast rice extract.

The most ominous adverse reaction, however, is *statin-associated dementia*. This syndrome has been documented by several research reports in the scientific literature, and thousands of anecdotal reports. The “statin effect study,” where patients on statins self-report side effects, tells us that 48% of patients on statin drugs report some degree of mental impairment. Statin-associated memory loss, difficulty concentrating, cognitive impairment, and global and partial amnesia are the dark side of statins. One might reasonably wonder are these problems ignored? The docs are thrilled to see their patients’ cholesterol come down, and the pharmaceutical companies love the cash cow.

The story of Millie, one of my patients, comes to mind. Millie had been misplacing her keys, losing track of what she was doing, getting disoriented, easily confused, and depressed. I told her about statin-associated dementia, and suggested she try going off her statin for a while. Within a week her brain started functioning again and all her symptoms went away. But then she had a cardiology appointment and when she told him what she had done and why, he fussed and fumed, called it balderdash and horsefeathers, and told her to get back on the drug. She did, but within a week, her cognitive and memory problems had returned in full force. Millie quit again, this time for good.

Take Renewal Research: 600 mg capsules. Take 1-2 capsules twice daily)

Phytonutrients

These include proanthocyanidins, flavones and polyphenols—fancy names for the plant-derived anti-inflammatory biochemicals—the medicine in food. For more information, read chapter 25, “The Phytochemical Revolution,” in my book, *Renewal: The Anti-Aging Revolution* (Rodale Press and St. Martin’s Press). Examples include pycnogenol, red grape extract (proanthocyanidins), bilberry extract (anthocyanosides and flavonoids), green tea (polyphenols), ginkgo biloba, milk thistle, and citrus bioflavonoid complex. Phytonutrients collectively exert powerful restorative effects on blood vessels, protect the delicate endothelium from inflammatory damage, and lower CRP. Focus on products that combine numerous phytonutrients in one capsule. (e.g., Phytonutrient Complex, Renewal Research; 1-2 capsules once or twice daily).

Multivitamin

Take the full daily recommended dose of a high quality multivitamin. The December 15, 2003 issue of *The American Journal of Medicine* published an article by Timothy S. Church, M.D. entitled “Reduction of C-Reactive Protein Levels Through Use of a Multivitamin.” A *high quality* multivitamin supplement (we are *not* talking about the kind you get from drugstores, big box stores, and pharmacies here!) given to research subjects lowered their CRP by an average of 32%. The greatest reductions were observed in those with the highest CRP elevations.

Vitamin C

According to a recent study published in the *Journal of the American College of Nutrition*, vitamin C reduces C-reactive protein levels. Researchers at the University of California, Berkeley saw a 24 percent drop in C-reactive protein (CRP) levels in participants who took 1-6

grams a day of vitamin C for two months. (Use buffered vitamin C or Ester-C—2000-6000 mg a day.)

Vitamin E (as “mixed tocopherols”)

Researchers at Southwest Medical Center in Dallas found that vitamin E, at 1200 IU daily, reduced CRP levels by 30% in three months. When the E was discontinued, CRP rose back up to previous levels in two months. Be sure to get the “*mixed tocopherols*” type of vitamin E, the only kind that contains the CRP-lowering *gamma-tocopherol* fraction. The label should say “natural vitamin E.” If the label doesn’t contain the words “gamma tocopherol” (the isomer that must be present for a vitamin E product to be effective), don’t purchase it. (Take three 400 IU capsules daily.)

Fish oil

All fish oils are not created equal! Our planet’s seven seas are contaminated with evenly-distributed methylmercury; no fish or seafood escapes exposure. All fish oil products must therefore be treated to remove this mercury. Many manufacturers do not do this. Make sure your fish oil product is certified “mercury free.”

Many large scale studies, including a report published in the July, 2006 issue of the American Journal of Clinical Nutrition, have confirmed the correlation between a higher intake of omega-3 fatty acids and a reduction in C-reactive protein.

Dose: Marine Lipids, Renewal Research; 1-2—1000 mg capsules once or twice daily.

Flaxseed oil

The alpha-linolenic acid in flaxseed oil provides the raw material for our bodies to synthesize inflammation fighting prostaglandins (Barlean’s brand; one tablespoon or six 1000 mg caps daily).

Coenzyme Q-10

An important free radical scavenger and mitochondrial energy production molecule, coenzyme Q-10 protects us from the free radicals that generate CRP. Our bodies make Coenzyme Q-10 when we are young, but production drops off dramatically after age 35. Need for this important molecule increases with age, however, so supplementation is recommended at middle age and beyond. In addition, patients taking statins—including the safe statin, red yeast rice extract—are at risk of coenzyme Q-10 depletion and should take 50-100 mg daily. Use the more bioactive reduced form, Coenzyme QH. (Renewal Research; 1-2—50 mg capsules once or twice daily.)

Vitamin D

Low blood levels of vitamin D have been linked with high concentrations of CRP (Take 1000-5000 IU daily. It is important to test 25-hydroxyvitamin D levels to make sure you are not getting too little or too much. Ideal range is 50-100 ng/ml.)

Magnesium

A Harvard/Brigham and Women's Hospital examination of 11,686 women participating in the large-scale Women's Health Study showed that high magnesium intake correlates with significantly lower C-reactive protein levels. Take 400-1000 mg/day. (Magnesium may cause loose stools in some individuals.)

Vitamin B-6 (as the bioactive form: P-5-P; pyridoxine-5-phosphate)

Studies have shown that a shortfall of this important B-complex vitamin will drive up C-reactive protein levels. P-5-P supplementation lowers CRP.

Daily exercise

The more you exercise, the lower your CRP will be. Shoot for one hour every day. There is no way around the fact that exercise is essential if you want a healthy heart. The Centers for Disease Control and Prevention published the results of a study of 14,000 people in the journal *Epidemiology* in September, 2002 (Vol. 13 No. 5) showing that a vigorous daily exercise program lowers CRP. The study examined various levels of activity, and showed that leisure-time physical activity was inversely associated with C-reactive protein concentration in a dose-response manner. That means the more you exercise, the more you lower your CRP. Combine strength with aerobic training. Vary what you do. Dr. Kenneth Cooper, founder of the world-renowned Cooper Aerobic Center in Dallas, has demonstrated—in numerous research publications and in a presentation of his research results to Congress—that vigorous exercise lowers CRP.

Diet to lower CRP

Low carbohydrate diet

Sugary and high carb foods dramatically increase the amount of inflammatory activity in your body and drive up your CRP. Foods with a high glycemic index will rapidly raise your blood sugar levels. These include most breads and baked goods, corn, potatoes, rice, most cold cereals, and all foods made with refined flour or added sweeteners. Avoid all sugars and sweets. Make antioxidant-rich fruit and vegetables your top food choices.

Low glycemic index foods include: all vegetables, lean meats, soy foods and tofu, beans, whole grain pasta, oatmeal, sprouted grains, whole rye bread, whole wheat pita bread, and corn tortillas. Even though you are limiting your intake to low glycemic index foods, always also try to combine equal amounts of protein and carbohydrate in any given meal. (See Chapter 11: Blood Sugar, Insulin Resistance, and The Metabolic Syndrome for information about low carb diets.)

Eat lean

All fatty foods, and especially saturated animal fats, cause inflammation and push up your CRP. Reduce or eliminate fatty meat consumption. Choose only the very leanest cuts of meat.

Skin-free organic chicken or turkey are low fat choices. Use nonfat or low fat dairy products. Avoid fried foods.

Lifestyle factors that lower CRP

Weight loss

If you are overweight, shedding some pounds will lower your CRP. Obesity is accompanied by low-grade inflammation that is linked—via higher CRP levels—to accelerated atherosclerosis and the metabolic syndrome.

Get rid of periodontal disease (gum infections)

Poor oral hygiene and periodontitis are associated with increased risk of cardiovascular disease. According to Paraskevas et al in a 2008 issue of the *Journal of Periodontology*: “There is strong evidence that plasma CRP in periodontitis is elevated compared with controls.”

According to the Dean of Dentistry and Head of the School of Dental Sciences, Newcastle University (as quoted in the *British Dental Journal*) “There is increasing evidence that reducing the inflammatory component in the periodontal tissues does have potential systemic effects. This has been shown to improve hyperglycaemic control in diabetics...and may be of benefit in patients suffering from coronary heart disease.”

Chronic low grade periodontal infections leak bacteria into the bloodstream. This drives up your CRP and can cause infections in the coronary arteries.

The bacterium *Chlamydia* is frequently found in infected gums, so if you have gum disease and an elevated CRP, have your doctor test you for anti-*Chlamydia* antibodies (IgG, IgA, IgM). If present, this bug responds to antibiotics.

Brush after every meal, floss daily and have your teeth cleaned by a professional every three months.

Additional methods to lower C-Reactive Protein

DHEA (dehydroepiandrosterone)

DHEA is an adrenal hormone that plays a critical role in regulation of inflammation. Optimum DHEA-S (we measure the sulfate form of DHEA on testing) levels are crucial for heart health and for keeping CRP low. The only way to know if your DHEA level is low is to test your blood for DHEA-S. If levels are below normal, take a DHEA supplement. DHEA is also an important anti-aging hormone. For a thorough discussion of the importance of DHEA for slowing the aging process, please read chapter 33, “DHEA and Pregnenolone: The Anti-Aging Superhormones,” in my book *Renewal: The Anti-Aging Revolution* (Rodale Press; St. Martin’s Press). Note: the normal range for DHEA-S is 500-800 mcg/dL in men and 300-500 in women. If you are below this range, supplement with 25 mg once or twice daily and retest in two or three months to make sure your level has come up into the normal range.

Improve glycemic regulation

Inflammation (as measured by a CRP elevation) is intimately connected to—and often seen with—fasting blood sugar elevation and the metabolic syndrome. This is because high blood sugar generates a variety of unwanted chemicals and hormones that cause inflammation.

A low carb diet and one hour of daily exercise are necessary to control insulin resistance and to reverse the metabolic syndrome.

Reduce blood iron levels

Excess iron—beyond that needed to make adequate hemoglobin—is a free radical looking for a place to do some damage. Iron causes oxidative stress (e.g., it can oxidize LDL particles) and that raises your CRP level. High iron levels are associated with increased risk of cancer and heart disease. Test for serum iron, ferritin, and TIBC (total iron binding capacity) to determine whether you have an iron overload. Results should be within standard normal range. You can lower your elevated iron by simply donating a unit of blood.

Find and treat infections

Inflammation and/or infection anywhere in the body will raise CRP and heart disease risk. The most common places for infections are the gastrointestinal tract, urinary tract, respiratory system, skin, and gums.

Other safe inexpensive natural medicines to lower CRP

- **Phytosterols**
- **Ginger**
- **Proteolytic enzymes**
- **Irvingia gabonensis**

Don't smoke

If you do smoke, quit.

Avoid these factors that cause elevation of C-Reactive Protein

- **Free radicals**, caused by:
 - **Fatty foods**: meat, fish, full fat dairy, and a high animal fat diet
 - **Trans-fats and hydrogenated vegetable oils** (other plant based oils—such as olive and soybean—are fine)
 - **Chemical pollutants**: chlorinated water, air pollution, industrial chemicals, pesticides, herbicides, food additives, perfumes
- **Avoid all seafood**. The oceans all contain high levels of methylmercury, and *all seafood* contains toxic levels of mercury—which, like all toxins, is a pro-inflammatory irritant. Mercury damages your immune system and is toxic to the central nervous system. Don't believe me? Look through a microscope at mercury-induced neuronal degeneration by going to http://www.youtube.com/watch?v=VImCpWzXJ_w. The video depicts a fish serving-sized dose of mercury destroying brain cells.

- **Radiation**
- **Smoking** and smoke
- **Alcohol** consumption
- **Sugar**
- A **diet deficit in antioxidants**, i.e., lacking in sufficient fruit and vegetables and other high-antioxidant foods
- A diet containing **suboptimal levels of vitamin C, flavone compounds, vitamin E, alpha lipoic acid, and coenzyme Q-10**.
- **Free radicals**—for a lengthy discussion and more extensive listing, read chapter 2 in my book: *Renewal: The Anti-Aging Revolution*.
- **High blood pressure**

Drugs that lower CRP*

- Aspirin
- Statins (use Red Yeast Rice Extract, the natural statin)
- Beta blockers (a type of medication for treating hypertension; if you must use a beta blocker to lower heart rate or blood pressure, use the gentlest: propranolol)
- ACE inhibitors
- Fibrates
- Niacin (high dose)
- Rosiglitazone®

* I don't recommend taking these; they are included for informational purposes only.

Chapter 9

Homocysteine

Sandblaster From Hell

Chuck has a busy week

Five years ago, Chuck Holmes was at the top of his game. His uncanny ability to crank out one astonishing achievement after another in the high tech world of computer programming and digital design had catapulted him into the highest realms of geekdom. In 30 years he had progressed from 80's whiz kid to primo west coast web designer.

Youthful, exuberant, creative, and generous, Chuck smiled and joked his way into people's hearts. Everybody liked him. You know the type: bright but not obnoxiously so, ready to help,

usually the center of attention, and always able to summon an incisive comment that cuts to the core of the matter.

Chuck worked hard and played hard. He was in love with his wife and his two boisterous teenage boys. His diet was ideal: plenty of fruit and vegetables, whole grains and beans. All organic. Low carb, no sugar, no white flour. Almost no animal fat. Trim and fit, Chuck played tennis on the days he didn't work out at the gym.

Chuck paid close attention to his health and it seemed perfect. He saw his doctor for regular checkups and his lab tests always came back normal.

Healthwise, he did everything right....or so it seemed.

Then, suddenly, one sunny Monday morning on the way to his office, Chuck felt a sharp pain in his chest. He collapsed and was taken to the ER, where he was told he was having a heart attack. An angiogram the next day revealed major atherosclerotic disease affecting all four coronary vessels. The next day a quadruple bypass was performed on him. Chuck had had a busy week.

In an office visit between his heart attack and his bypass surgery, Chuck rather pointedly asked his internist, "My cholesterol and LDL have always been normal. My HDL is high. On several occasions you've told me that I had the 'heart of a racehorse,' and that my coronary risk factors were 'very low.' Now this! What went wrong?"

Dr. Turner replied, "I am so sorry, Chuck, but I honestly don't know. Some people who have normal cholesterol levels still can have heart attacks." (By now I hope you realize what an understatement that was.)

Chuck wasn't getting helpful answers from his regular doctors, so he decided to enlist my help. I tested him, and discovered that his homocysteine had gone through the roof.

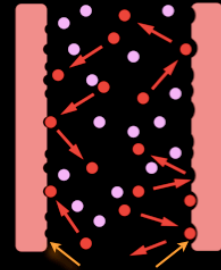
So what was it that caused Chuck's coronaries to harden? It wasn't cholesterol; his was low. It wasn't a sedentary lifestyle; he was active. It wasn't obesity, his weight was perfect. It wasn't diet; he ate right. The answer is that Chuck had a very common (but rarely diagnosed) disorder known as hyperhomocysteinemia—a five dollar word for too much homocysteine in the bloodstream.

What the heck is homocysteine, why is it dangerous, and why did Chuck have too much of it?

Homocysteine

“Sandblaster From Hell”

- **Homocysteine is an amino acid that is normally present in the human body. Certain B-complex vitamin deficiencies make it go up. When elevated, homocysteine becomes a powerful risk marker for heart and cardiovascular disease, and many other diseases.**
- **Excess homocysteine molecules crash into inner (endothelial) lining of arteries causing inflammatory damage and atherosclerosis.**
- **Excess homocysteine caused by B-complex vitamin deficiency.**
- **Excess homocysteine causes “platelet aggregation” (clotting), which increases risk of heart attack or stroke.**
- **Elevated homocysteine can cause coronary arteries to go into spasm.**
- **Normal level: ≤ 6.3 mg./liter.**
- **Treatment to lower homocysteine:**
 - **Folic acid** as Methylfolate 1000 mcg. capsules 1-2 twice daily.
 - **Vitamin B-6 (P5P)** 250 mg. of pyridoxine and 25 mg. of Pyridoxal-5'-phosphate 1-2 capsules daily.
 - **Vitamin B-12** 1000 mcg. tablets. Take three sublingual tablets daily.



Damaged inner arterial lining
● homocysteine
● other blood components
Homocysteine molecules crash into inner (endothelial) lining of artery causing inflammatory damage and atherosclerosis

What is homocysteine?

Homocysteine is a small, sulphur-containing amino acid molecule that our bodies generate in the process of recycling the essential amino acid methionine. Why be concerned about an obscure molecule that's part of an equally obscure biochemical process? Because a little too much homocysteine in your bloodstream can cause many diseases, and it can even kill you. In this section I will describe how homocysteine damages the heart and vascular system. In the following section, I will enumerate the many other diseases that are either caused or exacerbated by excess homocysteine.

As you know from Chapter 5, the endothelium—that delicate, one cell thick inner protective lining of our blood vessels—is continuously exposed to thousands of potentially damaging chemicals floating in the bloodstream. These irritants cause heart disease. Homocysteine, because it attacks and destroys important vascular protein molecules, is one of the nastiest.

Low levels of homocysteine are normally present in the human body. However, as long as levels stay below $6.3 \mu\text{mol/L}$, they won't cause any damage. When homocysteine rises above this safe cutoff point, the endothelium begins sustaining major damage. Like a powerful mini sand blaster, billions of homocysteine molecules crash into endothelial cells, irritating and damaging them. A chronically irritated endothelial lining loses its integrity and can no longer protect the layers of artery beneath it. The borders between the endothelial cells weaken, and begin allowing cholesterol-laden oxidized LDL particles and other pro-inflammatory chemicals

to squeeze past and gain access to the arterial wall (the *intima*) beneath. Over time this molecular pounding results in arterial inflammation, plaque, atherosclerosis, and thromboembolic disease.

Many diseases are associated with excess homocysteine

“Is homocysteine useful for predicting anything other than heart disease risk?” asks Chuck.

“Yes, it is. The homocysteine story doesn’t just end with heart and cardiovascular disease. Homocysteine doesn’t limit its vandalism to injuring arteries; it can cause inflammation anywhere and everywhere in the body, and this means that those with a high homocysteine are at higher risk for a striking array of diseases, including (but not limited to) macular degeneration, Crohn’s disease, ulcerative colitis, inflammatory bowel disease, aortic aneurysm, depression, bipolar disorder, schizophrenia, cervical cancer, Parkinson’s disease, and even birth defects.”

“Birth defects?”

“Well, Chuck, there’s no reason to think a fetus can’t be adversely affected by too much homocysteine.”

“I guess not.”

“Also, a buildup of homocysteine has an especially deleterious effect on sensitive brain tissue and cerebral function. High homocysteine levels damage the brain by fracturing important neuronal proteins and by ravaging the brain’s arterial supply lines. There is a close association between high serum homocysteine levels and neuropsychiatric disorders. Many studies have found a connection between hyperhomocysteinemia and impaired cognitive performance.”

“You mean it could cause senile dementia?” asks Chuck.

“Yes, alterations in cognitive function are seen in people with elevated homocysteine, ranging from mild cognitive decline—age-associated memory loss—to vascular dementia, and other senile brain syndromes including Alzheimer’s and Parkinson’s. A homocysteine level above 14 amplifies your risk of Alzheimer’s and other neurodegenerative disorders by a whopping 150%. Physicians often misdiagnose these changes as “normal aging,” but they are a preventable, reversible phenomenon.”

“Anything else homocysteine can do?” asks Chuck pensively.

“Numerous researchers have identified an association between cancer and impaired homocysteine metabolism. By disrupting collagen formation in bone, high homocysteine levels double the risk of osteoporosis. Population studies have shown that the higher a person’s homocysteine level the shorter their life expectancy. I could go on and on, but you get the idea. It affects everything.”

Widespread damage

The damage caused by homocysteine extends far beyond the cardiovascular system. As mentioned above, homocysteine excess is causally associated with body-wide risk for a plethora of chronic diseases, including osteoporosis, memory loss, cognitive impairment, senile dementia, Alzheimer’s disease, diabetes, fibromyalgia, chronic fatigue syndrome, birth defects, depression, rheumatoid arthritis, multiple sclerosis, and cancer. Though this is a disparate group of disorders, the fundamental pathogenic mechanism is the same: a toxic molecule (homocysteine) irritates and damages sensitive protein molecules. This triggers a chronic inflammatory reaction that causes ongoing cellular damage. When nerve cells are targeted, the result is Alzheimer’s, senile

dementia, multiple sclerosis, memory loss, depression, etc. When bone cells are damaged, we see increased fractures in the elderly. When joints are attacked, you get arthritis, and when a developing fetus is the target, we see birth defects. When cells of the cardiovascular system are ravaged by too much homocysteine, we see heart attacks, strokes, and other vascular diseases. The following brief summary of research results from thousands of studies depicts the tip of a huge iceberg:

Osteoporotic fractures in the elderly are far more frequent in those with high homocysteine. Women with high homocysteine levels have significantly lower hip bone mineral density than controls.

Cognitive function is affected by high homocysteine levels. Numerous studies have linked elevated homocysteine levels to vascular dementia and **Alzheimer's disease**. **Dementia** has also been associated with reduced levels of folate and vitamin B12.

High homocysteine levels are associated with increased risk of several **complications of pregnancy**. Abnormal homocysteine affects the developing fetal nervous system causing **neural tube birth defects**. In one large study, scientists found that pregnant women with the highest homocysteine levels had an increased risk of premature births, low-birth-weight infants, and stillbirths. Folic acid supplements have been shown to help prevent these birth defects.

Women with higher homocysteine have a significantly higher risk of **colorectal cancer** and **cervical cancer** than women with lower levels.

High levels of homocysteine predispose individuals to **inflammatory bowel disease**: ulcerative colitis and Crohn's disease.

More than half of patients with severe **depression** had elevated homocysteine levels and decreased levels of folate.

Young men with **bipolar (manic depressive) disorder** have higher homocysteine levels.

Many **schizophrenia** patients have high homocysteine levels. When vitamins were used to reduce the homocysteine, their symptoms of schizophrenia lessened.

Patients with age-related **macular degeneration** have higher homocysteine levels than healthy subjects.

From the above it becomes clear that anyone interested in optimum health and longevity would do well to check their homocysteine level and correct it with natural medicine if elevated.

Where does homocysteine come from?

Methyl (CH₃) groups—simply a carbon atom surrounded by three hydrogen atoms—are basic building blocks our bodies use in protein synthesis. We need a continuous supply of methyl groups to generate the tens of thousands of proteins our DNA is programmed to deliver.

Methionine, an amino acid in foods we eat, carries and delivers methyl groups. We call this “*methylation*,” and methionine acts as a “*methyl donor*.”

If we are nothing else, we humans are huge protein-synthesizing factories. (I don't want you to think that this is *all* we can do, but it is a good start.) Our genes are programmed to make the enzymes (which also are proteins) that catalyze the synthesis of vast numbers of proteins used for every conceivable bodily function, including organ and tissue maintenance, hormone synthesis, immunity, stress control, inflammation management, and healing. Proteins are likewise in great demand for repairing, removing, and replacing old or damaged cells. Methylation is a crucial part of this process. To supply enough methyl groups for all the proteins that are being

synthesized to maintain and repair our bodies, we need to be able to methylate—and recycle methionine—like crazy.

The methionine recycling pathway, one of thousands of biochemical pathways, provides an especially important biochemical function because it stores and delivers one of our bodies' most basic chemical building blocks: methyl groups. Here's how the methionine recycling pathway works. When methionine "delivers" a methyl group, it becomes S-adenosyl-methionine (SAME), which now needs to be recycled back into methionine. On the way back to becoming methionine, SAME can be converted into one of two amino acids: homocysteine (which we know is damaging) or cysteine (which is harmless). If conditions are right (and this is a big "if" as you will soon see), homocysteine is instantly converted back into methionine, which, now replenished, can go back out and deliver more methyl groups. Inadequate supplies of three B-complex vitamins—folic acid (as L-methylfolate), B-6 (as pyridoxine-5-phosphate), and B-12—will stall the recycling process, causing unwanted homocysteine to build up in the bloodstream. A long-term deficiency of B-6, folic acid, or B-12 causes a homocysteine buildup. It's like that famous "I Love Lucy" episode where Lucy and Ethel get a job in the chocolate factory and they can't keep up with the production line. Homocysteine, like the chocolates on Lucy and Ethel's conveyor belt, backs up, overflows, and spills out into our bloodstream—and that spells trouble. Like billions of tiny angry sharks, excess homocysteine molecules ravage the inner endothelial lining of our arteries, causing damage, inflammation, dysfunction, cell proliferation, plaque, clot formation, atherosclerosis—and, ultimately thromboembolic disease.

Mainstream and alternative doctors agree that simply replacing the trio of B-complex vitamins (using optimum doses, of course) usually solves the problem. Less often (about 15-20% of the time), a shortfall of choline, S-Adenosylmethionine, trimethylglycine, and/or zinc is responsible for the obstruction in methionine recycling. I'll discuss these in the section on treatment.

Misunderstood by mainstream doctors

No one questions that B vitamins lower homocysteine levels, but does this lowering translate into disease prevention or reversal? This idea has never been appropriately tested. Two major studies (Bonaa, NEJM 2006 and Albert et al., JAMA 2008), however, have succeeded in misleading physicians into thinking that homocysteine reduction is useless. In the first study, the Norwegian Vitamin Trial (NORVIT) published in the New England Journal of Medicine in 2006, Bonaa et al. reported on almost 4000 individuals with late-stage heart disease who had been recruited within a week of having experienced a myocardial infarction. These patients suffered from advanced cardiovascular disease—the kind that has been brewing for decades. Most of the subjects had normal homocysteine levels. After giving these patients small doses of B vitamins for two months, the authors concluded that this treatment was ineffective for reversing heart disease. A random person on the street could tell you it's unlikely that B vitamins could cure heart disease at all, much less in two months. Does it strike you as odd that none of the 100 doctors participating in this study realized how ludicrous this idea was?

A second study, published a couple years later (Albert, JAMA 2008) tried giving B vitamins to women at high risk of cardiovascular disease, again with the deluded expectation that vitamins could cure them. Multiple risk factors had been traumatizing these patients' arteries for decades, causing oxidative stress, inflammation, endothelial cell damage, endothelial

dysfunction, plaque formation, thrombosis, and cell proliferation—finally causing so much cumulative damage that a blockage in a major coronary vessel had occurred. B-complex vitamins—properly prescribed—might have helped prevent these infarctions, but it's a bit of a stretch to expect reversal of extensive damage. Providing B vitamins to heart attack victims would be about as likely to help as handing out tinker toys to after a tornado and expecting rebuilt homes.

Though there were multiple flaws in this study (see below). The most egregious, I believe, was the failure to examine and document all the heart markers discussed in this book. Heart attacks are multi-causal events, but Albert's study was based on the scientifically unsupportable—and truly unreasonable—assumption that all heart attacks are caused by B vitamin deficiencies and/or too much homocysteine. Failure to identify and address all the factors that caused their patients' disease doomed this study from the git-go.

There is no shortage of misguided research studies out there, and here we have two blatant examples. These studies proved what any reasonable person would expect: administering B vitamins to people who have just had a heart attack will produce no cures. Lowering homocysteine clearly helps *prevent* heart attacks and strokes (and senile dementia, osteoporosis, fibromyalgia, arthritis, cancer, etc.), but no expert in nutritional biochemistry would suggest that vitamins could *cure* them. Unfortunately, these high-profile studies deluded many doctors. Homocysteine-lowering as a way to prevent major cardiovascular casualties was stoned back to the Dark Ages. Here are the fundamental reasons why these studies should be tossed into the medical research trash can:

1. Most of the patients in these trials had normal (as defined by mainstream standards) baseline homocysteine levels.
2. The Bonaa researchers administered B vitamins as if they were a drug that could somehow quickly (two months) reverse decades of arterial damage in a patient population with advanced disease. A better understanding of underlying molecular biological processes would have revealed this misconception and led to a better study design.
3. Convincing evidence (Aklizhanova et al, 2008) indicates that the Albert study population was not even deficient in B-complex vitamins; this suggests other causes for their heart attacks.
4. Subjects in the Bonaa study had experienced a heart attack in the week before they were enrolled in the study. Nutrients like these B-complex vitamins work slowly and protectively; their role is preventive. They are not drugs and have no role in the treatment of acute life-threatening disease. The expectation that administration of B vitamins would somehow reverse life-threatening acute cardiovascular disease in severely ill patients reveals a significant misperception of scientific reality.
5. Inability to *reverse* (this is what both of these studies looked at) does not, by any stretch of the imagination, imply inability to *prevent*. In other words, administration of B-6, B-12, and folic acid to identical populations in the months and years *prior* to the study would probably have prevented many of these heart attacks, *but only in those deficient in these nutrients*.
6. Cardiovascular disease in both study populations was caused by combinations of other risk factors such as C-reactive protein, elevated fasting glucose, fibrinogen, or LDL particle size. To the extent these other factors played a role, homocysteine

reduction would have been useless, regardless of study design. None of these equally important causal mechanisms was addressed, and excluding them from the study betrays a certain naivety about the pathophysiology and biochemistry of atherogenesis (see Chapter 5).

7. Both study designs failed to address other known causes of elevated homocysteine: deficiencies of choline, SAME, DMG, and/or zinc.
8. Both were statistical studies rather than basic science research. Statistical studies are notoriously error-prone because they fail to address causality.

Studies have already shown—beyond any shadow of doubt—that homocysteine tears apart crucial cellular protein molecules, causing the horribly disfiguring nanoscale cellular damage that initiates atherosclerosis and numerous other disease processes. Hundreds of basic science research papers have already show that less homocysteine translates into less damage.

Meanwhile, the misconceptions persist and homocysteine remains the misunderstood Charlie Brown of biochemicals. Just about any conventional doctor will tell you these studies showed “B complex vitamins don’t cure patients with heart disease.”

Checking homocysteine saves lives

Information about homocysteine is widely available. Most doctors are at least aware of it. No expert questions that an elevated homocysteine can predict a future heart attack better than an elevated cholesterol. Had his doctor ordered this inexpensive test, Chuck’s homocysteine problem could have been diagnosed *before any symptoms appeared*, and a few cheap B-complex vitamins could have reversed his disease. Instead, homocysteine molecules beat up on Chuck’s coronary arteries for 20 years, corroding them and gradually setting the stage for a cardiovascular nightmare. All physicians should include an annual homocysteine level in their routine screening panel.

Chuck’s doc is not alone, however. Most physicians neglect to order a homocysteine level, an error of omission that in effect bestows a death sentence on millions of people—men and women alike—who, like Chuck on the way to bypass surgery, might be wondering why their doctor told them, “No worries; your cholesterol is fine.”

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*Chuck’s initial office visit was just a few days after his bypass. Before his visit, I had ordered my usual cardiovascular risk panel. All of Chuck’s risk factors but one were entirely in the normal range. The exception was his homocysteine, which was elevated at 18  $\mu\text{mol/L}$ .*

*In going over his results, I explained to Chuck: “Homocysteine is an ‘independent risk factor’ for coronary artery disease. Homocysteine is an amino acid molecule that is normally present in the body, and low levels of it are not going to hurt you. When levels rise, however, this molecule goes morphs into a killer.”*

*“What is a healthy homocysteine level, doc?”*

*“Homocysteine is measured from a blood sample taken after a twelve hour fast. A normal homocysteine level is at or below 7 micromoles per liter ( $\mu\text{mol/L}$ ). I like to see it below 6.3;*

above that number we start seeing risk. Based on a ton of research, that's optimum. Between 7 and 10 there is significantly increased risk, and risk gets very high above 10."

"What is my level?"

"Thirteen. That's high by anyone's standards."

"How does homocysteine damage my blood vessels?"

"Chuck," I explained, "the inner lining of your arteries—we call it the endothelium—is one cell layer thick. It acts as a highly selective membrane with two jobs. The first is to sort through all the chemicals floating in your bloodstream and allow passage of those that are desirable while keeping the unwanted ones out. The second job is to protect the arterial cells beneath it from irritants and toxic chemicals. This endothelial lining of your coronary arteries is very delicate and sensitive, and homocysteine molecules have been banging up against it for years now, causing inflammation and cumulative damage—in other words, plaque.

"Homocysteine," I continued, "also makes your blood more likely to clot, (technically we call this platelet aggregation) and this is not good because that clot—or thrombus—may block an artery and cause a heart attack."

"That's what happened to me?"

"Yes. Also, as a separate effect, homocysteine can cause coronary arteries to go into spasm, which is not what you'd want if the vessel were blocked by a clot."

"Oh, my," mutters Chuck.

"Yes, and it is appalling that your homocysteine hadn't been measured until now! It's far better at predicting cardiovascular disease than cholesterol, and there is no doubt that homocysteine played a significant role in your heart attack."

"If it's so important, why didn't my cardiologist—or my primary care doctor for that matter—why didn't they check my homocysteine out?"

"Good question. Wish I had a good answer."

"How do I get mine back down to normal?"

## **Lowering Chuck's elevated homocysteine**

"Lowering homocysteine is easy, inexpensive and virtually always effective. That's why it's such a shame yours wasn't checked earlier. Prevention is always easier than cure. This one little test could have saved you much grief. To lower your very high homocysteine of 15 down to the 5.0-7.0 that I'd like to see, I want you to take the following three B-vitamins: folic acid (as L-methylfolate 1000 mcg tablet, 1-2 twice daily), vitamin B-12 (as 1000 mcg 1-2 sublingual tablets twice a day), and vitamin B-6 (as pyridoxine-5-phosphate 50 mg capsules) 50-200 mg twice a day."

"How does it work?"

"These vitamins are coenzymes that facilitate the pathways that metabolize your excess homocysteine, breaking it down into methionine. A deficiency of the vitamins causes less homocysteine to be transformed back into methionine, so the homocysteine builds up in the bloodstream. Taking B-6, B-12 and folic acid revitalizes the transformation of homocysteine into methionine so your homocysteine level will gradually go down, and less homocysteine means less inflammatory irritation to the endothelial membrane and other sensitive structures throughout the body.

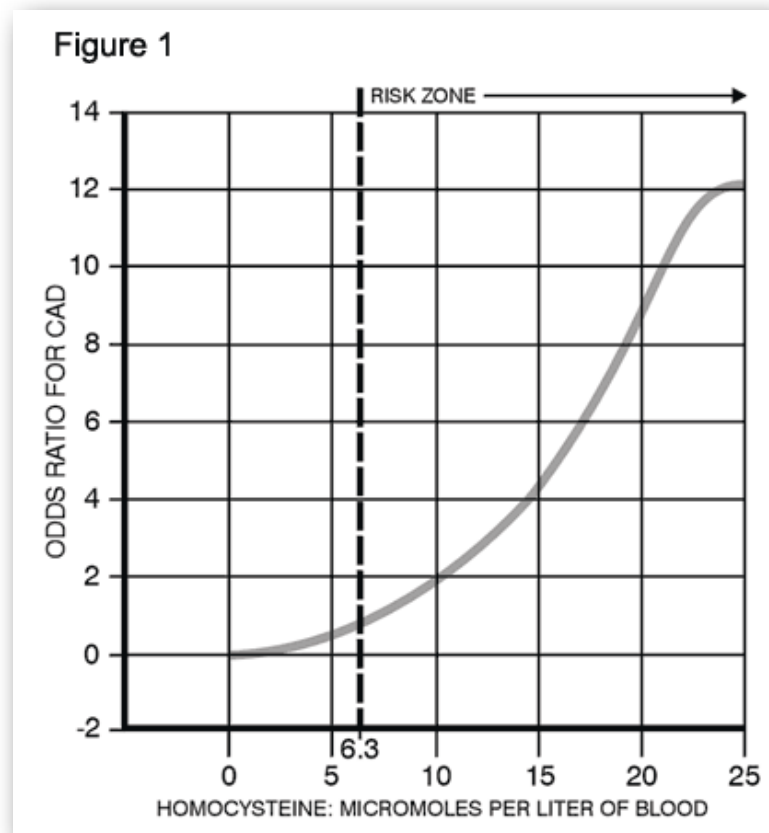
"Although," I continued, "most people respond to the standard triple vitamin regimen I just described, a small percentage is metabolically different and may need other nutrients (see

*Plans A and B below) to bring down their homocysteine. This is because there are several possible metabolic disruptions that can cause homocysteine to build up, so if after three months the standard treatment (folic acid, B6, B12) hasn't worked for you, don't give up. Simply try the other possibilities (listed below). Keep testing every three months and changing your program until you find the combination that works best for you. Don't settle for a slightly lower homocysteine! You want to get it down to 7.0 or less, and you want to keep it there permanently. This is the only way to assure zero risk of the many diseases caused by an elevated homocysteine."*

## What is optimum?

As seen in the graph below, risk gradually rises in tandem with homocysteine level. Experts choose to use a cutoff point of 6.3, below which there is no demonstrable increased risk of heart attack or stroke. Above 6.3, risk gradually rises. At 10, risk is about double baseline; at about 12 it is triple; at 15 quadruple.

Don't be surprised if the "normal" values for homocysteine that appear on laboratory reports and research studies are higher than the numbers I give here. This may be because the curve accelerates above 15 (i.e., is steeper) up to 25—but we are not statistics, we are individuals who desire optimum health, so even minimal risk is unacceptable.



*Coronary artery disease (myocardial infarction) risk rises with homocysteine level.*

## Homocysteine: poster child for a flawed approach to cardiovascular disease

The rest of Chuck's story is an inspiring medical success. He addressed the challenge of lowering his homocysteine with typical enthusiasm. He followed the treatment program (provided at the end of this chapter) and over the following nine months his homocysteine gradually returned to normal. Freed from the constant inflammatory damage, Chuck's coronary arteries slowly healed and he gradually got back to his life of work and travel. He returned to his busy computer consulting business, resumed his regular tennis, and booked a summer cruise to Norway with his wife and kids. It hadn't been too late to reverse the damage to his blood vessels.

Finding and treating his elevated homocysteine happened just in time for Chuck. Without treatment, his prognosis was less than rosy.

For the most part, Chuck's medical care had been superb: great docs, state-of-the-art CAT scans, EKGs, echocardiograms, angiograms, clot-busting drugs, and deft surgical techniques. Prevention, the most powerful medicine of all, had not been part of the picture. Beyond cholesterol measurement and a low animal fat diet, there had, in fact, been no prevention. This was unfortunate, though typical: mainstream medicine, for all its sophisticated technology, assigns lower importance to prevention than to treatment. Perhaps this is because there's less money in it, or because herbs and vitamins are poorly understood by conventional doctors. Whatever the reasons, our current system depends on a constant supply of new heart attacks, without which all that high tech equipment would just collect dust. The mortgage payment would still be due, but there'd be no revenue to cover it. Are you with me here? The monster is not happy when it is hungry.

Then there's the thrill of the heart attack (as long as it's not your own), the kind of medical excitement that drives millions to watch Gray's Anatomy reruns. With prevention, the thrill is gone; it's boring. How do you know you prevented *anything* (like, say, a myocardial infarction or a stroke) if it never happens? (Answer: for a specific person, you can't; for populations, you can.)

Chuck was lucky; he sidestepped the fate of millions. Senseless death is not the exception; it's the rule. Testing and treating, as outlined in this book, could prevent almost all heart attack deaths.

Though multiple positive risk factors generate even higher risk, an elevated homocysteine *alone*—that is, without an elevated cholesterol or LDL, and without elevations of any of the other risk factors for heart disease—can cause a heart attack or a stroke. Chuck was a perfect example. Conversely, lowering your homocysteine to 6.3  $\mu\text{mol/L}$  or less removes homocysteine as a risk factor, but will not negate the risk of a high cholesterol or an elevated CRP. Every “independent risk factor” must be addressed and treated. The more risk factors you identify and remove, the lower your overall risk of heart attack and stroke. Eliminating them all places risk at very close to zero.

# How to Lower Your Elevated Homocysteine

## Therapeutic Goal

Lower homocysteine to ideal level of 6.3 umol/L or less.

### Lowering Your Homocysteine Level

**L-Methylfolate**—an efficiently absorbed form of folic acid Dose: 800-1000 mcg. tablets. Take 2-4 daily.

**Vitamin B-6** (pyridoxine). Take as the active form, P-5-P (pyridoxine-5-phosphate). Best products combine pyridoxine with P-5-P in a 9:1 ratio; 275 mg. per capsule. Take 1-3 capsules daily.

**Vitamin B12** as methylcobalamin (important because other forms of B12 are not absorbed), 1000-5000 mcg daily (can be taken in one daily dose).

**Combined B12 methylcobalamin/methylfolate** products have recently become available (e.g., Renewal Research “Active B-12 - Folate”). These make dosing easier by combining in one tablet the most active, most absorbable forms of both folic acid (5-methylfolate) and B12 (methylcobalamine). Take 2-4 tablets daily, dissolved in the mouth or swallowed whole..

**It is important to take all three of the above B-complex vitamins, as the effects are synergistic.**

## Recommended program to lower your Homocysteine

As mentioned above, there are several possible biochemical causes of an elevated homocysteine. There is no test to determine which of these causes applies, so a little trial and error is required. The most common cause of elevated homocysteine (about 70%) is a deficiency of B-complex vitamins: folic acid, vitamin B-6, and/or vitamin B-12. Therefore, replacing these three vitamins is always the starting point. This is Plan A below. Most people will respond to the folic acid, B-6, and B-12 regimen.

To make sure your homocysteine-lowering program is on track, you will want to retest your homocysteine level every two months or so. Remember, homocysteine levels change slowly (we are talking months here), so you are looking more for a *direction of change* than for a normal result. In other words, if, compared to your previous result, your level is going down, even just a little, you know you are on the right track and that you should continue on your current program. If your retest level is not lower, then you are still not addressing all the possible biochemical causes of the nutritional deficiency that is causing your homocysteine to rise. About 15-25% of people will not respond to Plan A alone, so if you are not showing any response after two or three months, add the nutrients in Plan B. Testing every 2-3 months (until you establish that you are consistently moving in the right direction) will be necessary to determine which combination of nutrients you need.

### Plan A:

- **Folic Acid** as the *activated* form of the vitamin *L-5-methyltetrahydrofolate* or *5-methylfolate*, 800-1000 mcg capsules. Take 2-4 capsules daily (can be taken in one daily dose).
- **Vitamin B12** as *methylcobalamin* (important because other forms of B12 are not absorbed), 1000-5000 mcg daily (can be taken in one daily dose).
- Products have recently become available (e.g., Renewal Research “Active B-12 - Folate”) that make dosing easier by combining the active, absorbable forms of both folic acid (as 5-methylfolate) and B12 (as methylcobalamine). Take 2-4 tablets daily; dissolved in the mouth or swallowed whole.
- **Vitamin B-6** (pyridoxine)—as the active form, P-5-P (pyridoxine-5-phosphate). Look for a product that combines pyridoxine with P-5-P in a 9:1 ratio. If one capsule contains 275 mg. (a standard dose), take 1-3 capsules a day.
- Note that the B-complex vitamins above are different from what you would normally find in your multivitamin. You want L-methylfolate and pyridoxine-5-phosphate, the *activated forms* of these vitamins. Also, the doses, though still entirely safe, are higher than those in your multi.
- Because all B vitamins works synergistically, it is important to take a multiple vitamin (to ensure lower levels of all the B-complex vitamins) when on the above program. (You should be taking a multi already for general health.)
- Retest after 2-3 months. If homocysteine levels are going down, stay on this program. If no change (or it's higher), switch to Plan B.

## Plan B

If you are among the 15-25% of people who won't respond to the above Plan A regimen, your homocysteine elevation was not caused (at least not solely caused) by a shortfall of folic acid, B6, and/or B12. The focus now shifts to a possible deficiency of other nutrients that facilitate removal of excess homocysteine. These include choline, S-Adenosyl methionine (S-AMe), and trimethylglycine (TMG—also known as betaine, a B-complex vitamin). If a two month trial on these supplements lowers the homocysteine (even just little) you'll know a deficiency of one or more of these nutrients is part of your homocysteine problem. (Do not discontinue the P-5-P, methylfolate, and B12 during this trial as these may still be part of the problem.)

- **Choline** as phosphatidyl choline with associated phospholipids and nutritional cholinergic synergistic compounds. (Use Omnicholine from Cardiovascular Research; 2-4 capsules twice daily.)
- **S-AMe** (S-Adenosyl methionine); 200-800 mg daily.
- **TMG** (Trimethylglycine; Betaine HCl) 500 mg capsules. Take 500-3000 mg per day in divided doses. TMG is mildly acidic and helps digest protein, so take only with meals.

It is best to try all three of these nutrients together, because they reinforce each other's action. If, on retesting, you see a homocysteine reduction after 2-3 months, try going off one or two of the three to figure out which is working. If no homocysteine reduction in three months, discontinue all three, as they are not working.

It is important to appreciate that getting homocysteine to normal/baseline (i.e.,  $\leq 6.3$ ) is not the immediate goal here. That could take up to a year or more, as homocysteine levels move down very slowly. *Any* movement in the desired downward direction would indicate the nutrient combination you are taking is working and that you should stay the course.

## Additional nutrients that lower homocysteine

- **Zinc** (as citrate, picolinate, or aspartate). Take 30-90 mg daily.
- **Vitamin C** (1000-8000 daily of buffered C or Ester-C) and Vitamin E (400-1200 IU daily, as *mixed tocopherols* only). Homocysteine has been shown to increase free radical activity in endothelial cells. Vitamins C and E don't lower homocysteine directly, but as free radical scavengers they protect the endothelium from oxidative damage by homocysteine.
- Take a high quality **multivitamin** every day. (Please note: Big Box stores, food chains, and drugstore chains do not sell high quality multivitamins.)

## Avoid these factors that cause homocysteine elevation

- *High dose niacin* (only problematic at the higher pharmacologic doses used to lower cholesterol; no effect on homocysteine at doses found in vitamin supplement preparations).
- *Colestipol* (Colestid), a cholesterol lowering drug, raises homocysteine levels.
- *Tobacco* raises homocysteine.

## Drugs that lower homocysteine

No pharmaceutical product lowers homocysteine.



## *Chapter 10*

# **Fibrinogen**

## **Clotting Factor and Inflammatory Protein**

### **Elevated fibrinogen both predicts and causes cardiovascular disease**

Fibrinogen is a large sticky protein molecule that's intimately involved in blood clotting and inflammation management. It's manufactured by your liver.

Fibrinogen, a soluble protein, floats in the bloodstream. If bleeding occurs, it is transformed into a solid fibrous protein that becomes the scaffolding upon which a blood clot is formed. As a completely separate function, fibrinogen also functions as a messenger molecule that coordinates and regulates our bodies' response to inflammation.

We need fibrinogen. Like homocysteine, C-reactive protein, and cholesterol, this molecule—at normal levels—performs necessary and important functions in the human body. When we make too much of it, problems appear and these problems—as we shall see—have to do with clotting and inflammation.

Many studies have shown that elevated fibrinogen is a major risk factor for atherosclerosis; cardiovascular disease specialists no longer question its importance. Several decades of research have confirmed that persistently elevated fibrinogen levels predict heart attacks and strokes with exceptional accuracy. It is easy to see why this would be true: fibrinogen participates in just about every step along the way to developing an atherosclerotic blockage in the vascular system.

Many experts feel that fibrinogen may be the overall single best risk factor for predicting heart attacks and strokes. One prominent researcher has stated that an elevated fibrinogen raises heart disease risk by 600 to 900 percent. Elevated fibrinogen levels have also been linked to increased risk of diabetes, hypertension, and even cancer. Several researchers have shown that a high fibrinogen is associated with a sevenfold increase in deaths from all causes. Maintaining a normal fibrinogen level thus translates into huge health dividends.

### **Not an innocent bystander**

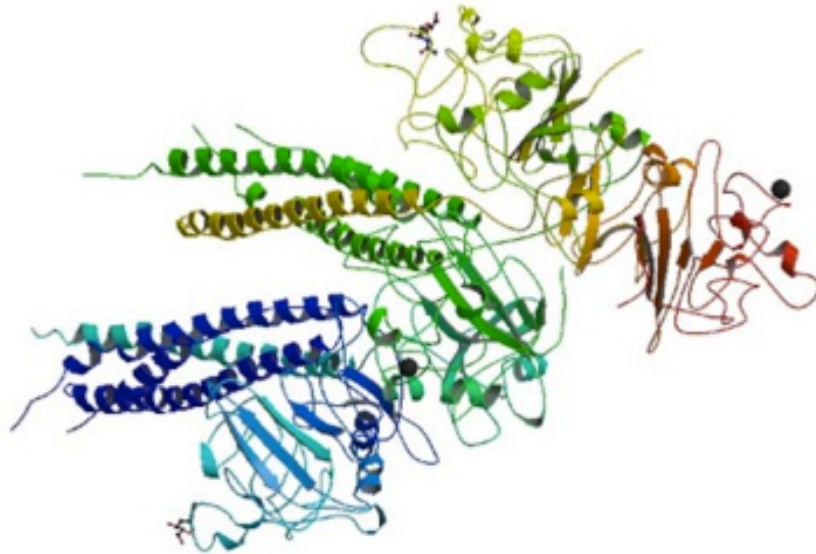
Fibrinogen is no innocent bystander that just happens to be hanging around when other factors cause vascular disasters. Fibrinogen, at normal (or “physiologic”) levels, behaves itself. Too much fibrinogen, however, and it morphs into a monster that actively participates in the

cellular destruction that leads to cardiovascular disease. At levels exceeding 250 mg/dL, fibrinogen launches attacks on the vascular endothelial lining and on the clotting system.

By causing exaggerated inflammation fibrinogen destroys the endothelium. This promotes atherosclerosis.

By promoting clot formation, excess fibrinogen obstructs major vessels. These local clots can become deadly blood vessel-blocking thrombi.

Fibrinogen's one-two combination punch of inflammation and clot promotion causes strokes and heart attacks. Yet, ironically, very few doctors order this test and even fewer know how to coax an elevated fibrinogen down into the normal range.



*Fibrinogen*

## **Brent Chadwick: an attorney with an elevated fibrinogen level**

*Here with me now in my consultation room is long time friend and patient Brent Chadwick, a 48-year-old San Francisco assistant district attorney. Vibrant, outgoing, and not without a sense of humor, Brent's a crusty barrister who's accustomed to adversarial courtroom dramatics, so instead of asking questions like a normal patient, he grills me as if I were a defendant. All he really wants is the truth.*

*I tested Brent's heart markers a few weeks earlier, and he's here to discuss the results. The only abnormal result on his Cardiovascular Risk Profile is an elevated fibrinogen.*

*"Doc, I Googled fibrinogen, and now I know that it's a clotting protein and an 'acute phase reactant.' Whatever that is. What does any of that have to do with my heart?"*

*"Well, Brent, fibrinogen is an important independent causative marker for atherosclerosis and coronary heart disease. In other words, high levels of fibrinogen predispose a person to*

*heart attacks and strokes, even though—as is true for you—cholesterol and all the other risk factors are normal.”*

*“Since everything else was normal on your battery of tests, how bad could it be? Couldn’t we just give me a pass on this one?”*

*“Sorry, Brent, but there is a reason we call these ‘independent markers.’ It’s because they act independently of one another. In other words an isolated fibrinogen elevation (or CRP or glucose or homocysteine or LDL) can and will cause atherosclerotic heart and cardiovascular disease all by itself.*

*“And just how good a marker is it?” he asks, in low, even, lawyerly tones.*

*“A very good one. High fibrinogen levels have at least as great a predictive value as any other marker. In fact elevated fibrinogen accounts for many of the heart attacks that happen to the 50% of heart attack victims who have healthy cholesterol levels. One major study involving over 2000 men showed that those with a low LDL cholesterol but high fibrinogen levels had six times the risk of a myocardial infarction than those with a low fibrinogen and elevated cholesterol.”*

*“That’s amazing!”*

*“Yes, it is. Of course if both cholesterol (or any other marker) and fibrinogen are elevated, one’s risk is very much higher than if it’s just one or the other.”*

*“What’s my fibrinogen level doc?”*

*“At 341, it’s well above the upper limit of the ideal range (150-250 mg/dL), and this tells me that you are at risk.”*

*“Of a heart attack?”*

*“Yes, or a stroke.”*

*“What is fibrinogen, anyway?”*

*“It is a very large protein molecule that commands a lot of respect.”*

*“Respect? Do proteins get respect?”*

*“This one sure does. It can both save your life and it can kill you.”*

*“How could it do both?”*

*“Normal levels of fibrinogen are important for blood clotting and managing inflammatory challenges to your body such as infections, allergies, and stress. But at high levels, fibrinogen morphs into a vandal. It damages arteries, accelerates atherosclerosis, encourages the formation of blood clots...”*

*“You mean the kind of clots that cause heart attacks?”*

*“Yes, but not just those, all kinds. Fibrinogen doesn’t know the difference between a heart attack and a cut finger...”*

*“I sure would if I were the one having a heart attack!”*

*“Well, Brent, I guess that proves you’re smarter than fibrinogen.”*

*“Touché.”*

*I just kept going: “Fibrinogen, you see, regardless of its IQ, floats along in the bloodstream as a soluble protein. When bleeding occurs, fibrinogen’s job is to plug the leak, and to accomplish this it possesses the unique capacity to change from its usual soluble form into an insoluble form called fibrin. Fibrin is sticky, so it adheres to the inside endothelial surface of the blood vessel forming the mesh-like matrix or scaffold upon which a blood clot can be built. It then snares passing red blood cells and platelets, forming a clot. Now if you have cut your finger, it is important that the coagulation process I just described occurs rapidly so you don’t lose much blood. If you are hemorrhaging, fibrinogen can save your life. Too much fibrinogen can*

*cause a disaster, though, by enhancing the probability of an unwanted clot that blocks blood flow to your heart or brain. That's why too much fibrinogen dramatically increases your risk of a heart attack or stroke. We want to avoid this at all costs."*

*"We sure do! So, does it really cause heart attacks, or is it just hanging around when they happen?"*

*Brent apparently now needs to determine whether fibrinogen is an innocent bystander or the actual killer. This is an excellent question.*

*"Fibrinogen participates in the process. It has been clearly recognized to be a killer. Let me put it this way, Brent: at the right level in your system, fibrinogen is a hero committed to protecting your life. Too much, however, and our savior mutates into a homicidal maniac."*

*An 'aha' smile creeps onto Brent's face, and I can tell that this is a way of putting it that he can wrap his legal mind around. Now he is going to start looking for the smoking gun.*

*"But you haven't told me exactly how it causes heart attacks and strokes. Since my level is elevated, I have a vested interest in your answer."*

*"Fibrinogen is involved at several different points. It causes endothelial irritation and inflammation. (See Chapter 5, Atherogenesis: How Arteries Fail.) It then continues to participate by incorporating itself into arterial plaque as it forms. Inside the wall of the artery, fibrinogen converts to its insoluble form, fibrin, which then serves as the scaffold that holds cholesterol in plaque. Fibrinogen is also incorporated into the foam cells that contribute to plaque.*

*"Outside the plaque, in the bloodstream, excess fibrinogen will increase the viscosity of blood, causing it to slow down—and when blood stagnates it is then more likely to clot."*

*"Kind of like when there's congestion on the freeway?"*

*"Why, yes, but then fibrinogen raises the ante by encouraging platelets to stick together (this is called platelet aggregation) where and when the traffic slows down. When platelets clump, you have a clot. This impairs local circulation and shuts off the local supply of oxygen and food to cells in the heart or brain. At its worst it can cause an abrupt total blockage of blood flow in that artery. That can spell sudden death."*

*"Whoa!"*

*"Brent, these kinds of arterial blood clots are the leading cause of death in the Western world. Every year in the U.S. alone, about 1,000,000 heart attack and stroke deaths occur as a result of blood clots obstructing the delivery of blood to the heart or brain."*

*"So I guess taking steps to reduce elevated levels of fibrinogen makes a lot of sense—perhaps could save one's life? Perhaps my life! Perhaps the lives of many many others."*

*"You bet."*

*"Millions of lives would be saved if doctors routinely tested and treated it!"*

*"They don't though."*

*"Why not? That'd be malpractice, wouldn't it?"*

*"One would think so, Brent, since we are talking about a marker far superior to the cholesterol we doctors routinely—almost religiously—check."*

*"So why don't they?"*

*"Doctors are unlikely to order a fibrinogen level because if it came back high, they wouldn't know what to do. When they spot a high cholesterol, they can write an Rx for statin drugs. But there is no 'statin' for fibrinogen." If a fibrinogen-lowering drug existed, you'd see medical journal ads, continuing education programs, research money for population studies, free samples, TV commercials—the whole enchilada. Unfortunately, however, the only medications that lower fibrinogen are plant-derived, food-based medicines. Big Pharma can't patent these*

*'nutraceuticals.' With no prospect for profits, there's no incentive to market natural products like nattokinase (a soybean derivative), curcumin, serrapeptase, bromelain, green tea, or garlic."*

*"I see. So the docs just refuse to order the test?"*

*"Yes. When asked to order a fibrinogen level, Brent, most doctors will tell you it's is a "newly identified" risk factor, so they need "more proof" before they'll order it. Fact is, hundreds of studies over the past thirty years have documented fibrinogen's status as a major risk factor. No cardiovascular expert now questions fibrinogen's atherogenic potential or its predictive power for heart attacks and strokes. It's an honest-to-goodness smoking gun for strokes and myocardial infarctions."*

*"And natural medicines do work to lower fibrinogen?"*

*"Yes, Brent. The ones I just mentioned are proven nutritional medicines that either lower fibrinogen or protect from its adverse effects, or both. Before we get you started on a program, however, let me explain a little more about what fibrinogen is and why it is important..."*

## **Fibrinogen plays major roles in inflammation management and clot formation**

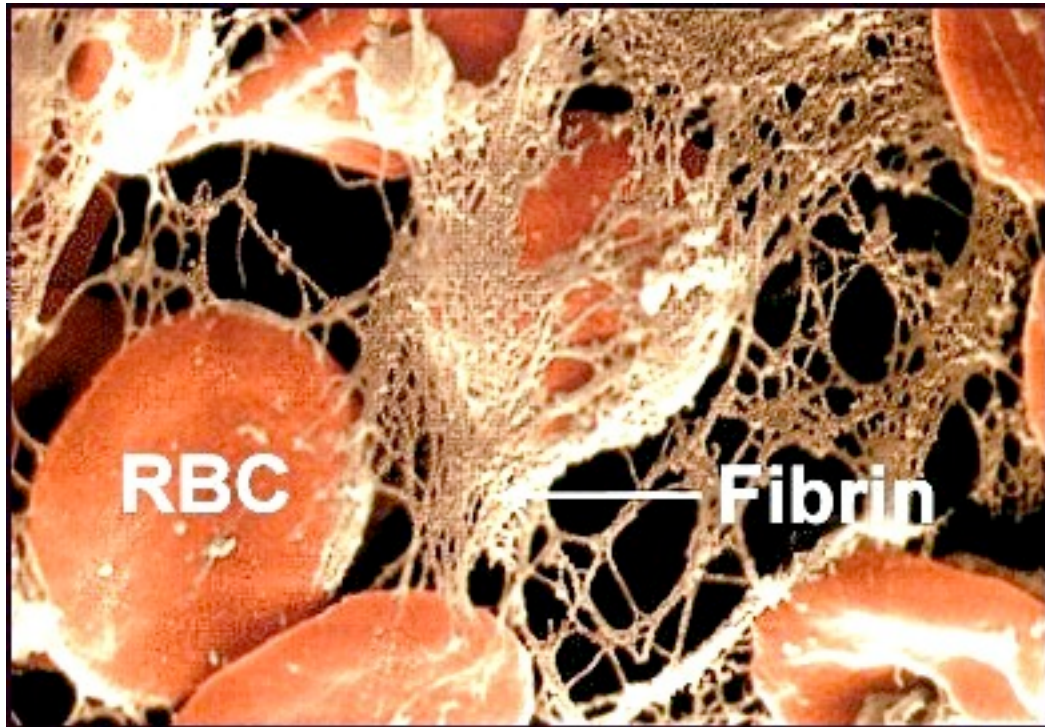
If one were to step back and scan the entire molecular biological landscape in search of the hottest smoking gun—the factor most intimately associated with heart attacks and strokes—one biochemical would stand out above a crowded field: fibrinogen. Why? Because fibrinogen is intimately associated with—and the driving force behind—inflammation and blood clot formation, the two processes that cause strokes and heart attacks. Fibrinogen directly causes inflammatory damage to the wall of the artery, setting the stage for atherosclerotic plaque and thrombus formation. And, in heart attacks and strokes, fibrinogen (a liquid) solidifies to form fibrin, resulting in an artery-blocking clot. The connection doesn't get any more intimate than that.

Fibrinogen has two main jobs in the human body. The first is as an inflammatory protein, an "acute phase reactant." Inflammation anywhere in the body triggers hepatic fibrinogen production. This protein is released and travels far and wide notifying various body systems that inflammation is afoot and providing explicit instructions about how to deal with it. Problem is, fibrinogen doesn't just manage inflammation; at elevated levels, it also *causes* inflammation. Elevated fibrinogen levels damage blood vessels, setting the stage for heart attack and stroke.

Fibrinogen's other job is to serve as the soluble precursor of fibrin, the solid protein that forms the scaffolding upon which a blood clot is built. Damage to an artery triggers the conversion of fibrinogen to fibrin, thus initiating a blood clot. This clot is usually necessary; our blood vessels are continuously sustaining damage from trauma (e.g. your daily workout) plus normal wear and tear. Local clotting is the first step in the healing process. These "healing clots" are short-lived, remain small, and serve to quickly restore the healthy artery wall. However, when arterial damage is sustained, regardless of cause, the clot may increase in size and become a thrombus—a larger, growing clot that can block a blood vessel. Excess fibrinogen increases the propensity to make clots. Not a good thing. Lower fibrinogen levels are associated with protection from unwanted clots.

## Excess fibrinogen causes clots and thrombi

Coagulation—the clotting of blood—is a complex sequence of biochemical transformations initiated by tissue damage and terminating with the formation of a blood clot. That clot’s purpose is to plug the hole and stop the bleeding. Coagulation is a tightly controlled process that protects us from excessive bleeding. In the final step of the cascade, fibrinogen (a soluble protein) is converted into insoluble fibrin, the long thin fibers that intertwine, forming a mesh that traps platelets and red blood cells to form a clot.



*Fibrin trapping red blood cells to make a clot.*

It is crucial that our bodies maintain a dynamic homeostatic balance between fibrinogen and fibrin within the clotting system. Fibrinogen is always changing into fibrin, but the fibrin formed is continuously dissolving and being recycled back into fibrinogen, so no clots form. As long as fibrinogen levels don’t get too high, this system works great. When this recycling process breaks down, however, fibrinogen levels go up. The excess fibrinogen irritates the arterial endothelial lining and damages it, causing local inflammation. Fibrinogen converts to fibrin and sticky fibrin fibers accumulate, providing a scaffold on the inside lining of the arterial wall that traps platelets and red blood cells to form a clot. This local injury and clot attract oxidized LDL-cholesterol, monocytes, cellular waste products, and an array of inflammatory molecules that coalesce into atherosclerotic plaque.

If the surface of a developing plaque continues to be irritated, the plaque grows in size and may rupture, causing more fibrinogen, platelets, RBCs, and other inflammatory chemicals to

accumulate at the site in an attempt to repair the injury. Under these conditions, the local clot grows larger and becomes a thrombus which gradually narrows and chokes off flow in the artery.

A thrombus might not initially block blood flow, but if a piece breaks off and travels downstream (now we call it a *thromboembolism*), it will come to rest in a narrower part of the vessel, where it completely chokes off the flow of blood, causing rapid tissue death and sudden, severe symptoms of a myocardial infarction or stroke. At this point, more often than not, someone dials 911.

## **Fibrinogen manages inflammation, warns of inflammation...and causes it!**

Besides clotting, fibrinogen has another main job, that of initiating, monitoring, and managing the inflammatory process.

You may have already noticed that life in a human body entails a more or less continuous onslaught of assaults coming from many directions. Just using our bodies to move around creates wear and tear on the joints, ligaments, tendons, and muscles. Add to that physical injury (trauma), microbial attack (we are continuously fighting off pathogens), allergens (most of us have food or inhalant allergies), and toxins (we do survive in a toxic environment).

Without a way to respond to all this damage we'd be in big trouble. Fortunately we (or, more specifically, our bodies) do have a "plan." Our response to all the different kinds of assault —trauma, infection, allergy, and toxins— is *inflammation*. Inflammation, in turn, triggers what pathophysiologists call the "acute phase response" or "APR." The purpose of the APR is to manage the inflammatory reactions, to respond to the damage, and to manage the healing process. The APR consists of an outpouring from the liver of a barrage of inflammation-managing "acute phase" proteins. The list of known APR proteins is very long and you have probably not heard of most of them: ceruloplasmin, serum amyloid A, alpha-1 antitrypsin, haptoglobin, interleukin (IL)-1 receptor antagonist, components of the complement cascade, hepcidin, ferritin, C-reactive protein...and our friend fibrinogen. Collectively these APR proteins provide enhanced protection against invading micro-organisms, limit tissue damage, enhance healing, and promote a rapid return to homeostasis.

We need the APR to handle difficult situations; it temporarily improves our adaptive and defensive capabilities. Next time you catch a cold, cut or bonk a finger, or develop a splitting headache, you can impress all your friends by telling them you have decided to have an APR. Not that there's actually a choice here. Literally anything that causes inflammation (including trauma, infection, toxins, allergens, arthritis, myocardial infarction, stroke, and various cancers) will cause a shift to the APR and heightened fibrinogen production.

Think of fibrinogen as like a herd of tiny horses, each one ridden by a little Paul Revere. When there's inflammation anywhere in your body, hepatic fibrinogen production increases, and gobs of it are released into the bloodstream. They float to the far-flung regions of your body shouting "Inflammation is coming! Inflammation is coming!"

The walls of blood vessels in the heart are especially sensitive to these fibrinogen messages. Prolonged levels exceeding 250 mg/dL cause the endothelial damage that initiates formation of both atherosclerotic plaque and thrombi.

Two chapters in this book are devoted to acute phase reactants: C-reactive protein, and fibrinogen—the two that also happen to be heart markers. This is not a coincidence.

## **If fibrinogen elevated, test more than once**

Sooner or later all of us will experience an elevated fibrinogen because we all get transient inflammation. We stub our toe, twist an ankle, shovel too much snow, play that extra set of tennis, have surgery, get a toothache, sinus infection, cold, or flu (infection). When we heal, the inflammation subsides, and the fibrinogen level comes down. The very presence of an elevated fibrinogen is synonymous with danger and damage. When considering cardiovascular risk, however, we are not interested in transient elevations. It's only a prolonged high fibrinogen level that causes atherosclerosis.

The only way to know if a fibrinogen elevation is acute or chronic is to test again (usually in 1-3 months). If fibrinogen is normal on repeat testing, we know it was a transient elevation and there is no need for concern. If it remains elevated, *regardless of the cause for the elevation*, treatment is necessary because persistent elevation causes arterial damage. Optimally, one would identify and treat the cause, but if that is not possible, it is still necessary to address the elevated fibrinogen and lower it with nattokinase, curcumin, and/or serrapeptase.

## **High fibrinogen especially dangerous when any other heart marker is elevated**

Researchers have discovered a biologically sadistic turn of events—if fibrinogen is elevated along with any other heart marker, atherosclerosis and heart attack risk skyrockets. Here's how fibrinogen works in cahoots with the other heart markers:

- LDL-cholesterol (see Chapter 7) - Risk of atherosclerosis is exponentially higher in people who have both a high cholesterol and a high fibrinogen. In a 1995 New England Journal of Medicine study, SG Thomson et al showed that in 3000 angina patients with coronary artery insufficiency (lack of adequate blood supply) if fibrinogen was low, elevations of cholesterol and/or C-reactive protein presented little risk, but when fibrinogen was high, heart attacks were far more likely.
- HDL-cholesterol (see Chapter 7) - Fibrinogen acts as the trigger for the atherogenic effect of a low HDL.
- C-reactive protein (see Chapter 8) - If your fibrinogen is elevated, your CRP is more likely to be elevated too—and vice versa. Production of these acute phase proteins is triggered by the same pro-inflammatory chemicals known as cytokines.
- Homocysteine (see Chapter 9) - An elevated homocysteine drives fibrinogen upward by blocking its breakdown.
- Fasting blood sugar and TMS (see Chapter 11) - Individuals with elevations of both fasting glucose and fibrinogen are at significantly higher risk of heart attack or stroke. Insulin resistance potentiates the adverse effects of an elevated fibrinogen and fibrinogen levels are significantly higher in patients with the metabolic syndrome. The good news is that low carb dieting, weight loss, and aerobic exercise will reverse insulin resistance and also lower fibrinogen.
- LDL particle size (see Chapter 7) - Elevated fibrinogen is more common in individuals with the “bad” (“B” or small dense) LDL particle size.



# Lowering Your Elevated Fibrinogen

## Therapeutic Goal

- Reduce fibrinogen level to 250 mg/dL or less.

### Lowering Your Fibrinogen Level

**Nattokinase**—a soy-derived “fibrinolytic” (clot-dissolving) enzyme that dissolves away the fibrin deposits upon which a thrombus (blood clot) might otherwise have been built. Do not use with other blood thinners. Discontinue use two weeks before scheduled surgery. Dose: 1-2 100 mg. capsules once or twice daily.

**Curcumin** (a component of the spice turmeric)—blocks hepatic fibrinogen production and addresses virtually every aspect of atherosclerosis. Dose: 2-8 500 mg. phytosome capsules twice daily, or use turmeric liberally in cooking. 2-8 grams a day have been used in research studies. Stick with “phytosome” products in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption.

**Serrapeptase**—an anti-inflammatory nutritional medicine that removes fibrin and fibrinogen by digesting it. Serrapeptase also selectively removes many other proteins that impede healing and optimum health. Dose: 2-6 enteric-coated capsules once or twice a day. Do not use with blood thinning drugs. Patients taking antibiotics should consult an alternative physician before taking Serrapeptase.

**Flaxseed oil**—1 tablespoon or 6-8 capsules daily.

**Green tea**—antioxidant; lowers fibrinogen—1-4 cups or 1-4 capsules daily

**Bromelain**—an anti-inflammatory enzyme; removes fibrin 1-4 capsules daily



*Natto beans*

## **Nattokinase**

Fibrinogen floats harmlessly in the bloodstream as a soluble protein, until it encounters chemicals that signal the need for a clot (such as those it would encounter in an inflamed endothelium). These transform it into its insoluble form: fibrin. Thick bands of fibrin stick to the endothelial wall forming a meshwork that snags passing red blood cells and platelets, becoming a blood clot. This clot is positioned exactly where we *don't* want one: inside a blood vessel.

Nattokinase to the rescue! Nattokinase, a soy-derived dietary supplement and “fibrinolytic” (clot-dissolving) enzyme, dissolves away excess fibrin deposits. This removes the fibrin scaffold upon which a thrombus could have been built. In the presence of nattokinase, thrombi (built on a fibrin scaffold), gradually shrink and disappear. Scientists call this “thrombolysis”—literally the “lysing” (or dissolving) of a thrombus. No prescription drug medication—not even Coumadin—is capable of thrombolysis.

Used safely in Japan for over 1000 years, nattokinase thins blood and outperforms pharmaceutical agents such as warfarin (Coumadin), Plavix, and heparin which merely thin the blood but are not capable of dissolving preexisting thrombi.

Taking nattokinase on a daily basis keeps fibrin under control and dissolves developing thrombi, thus preventing and reversing atherosclerosis. The risk of heart attack or stroke is dramatically reduced.

Research studies have shown that nattokinase is effective for a broad range of disorders including hypertension, peripheral vascular disease, intermittent claudication, hemorrhoids, varicose veins, chronic inflammation, pain, fibromyalgia, chronic fatigue syndrome, poor healing, retinal pathology, infertility, uterine fibroids, and endometriosis.

### **Clot buster**

The beauty of nattokinase is that it delivers the clot-busting benefits of powerful drug medicines like heparin, tPA (tissue plasminogen activator), urokinase, Plavix, and warfarin (Coumadin) without any side effects or adverse reactions. Anti-clotting drugs interfere with normal function, whereas nattokinase supports and improves the overall health and functionality of the clotting system. This food-based medicine—free of side effects and toxicity—supports Mother Nature rather than working against her.

### **Safety**

There have been no published reports of toxicity associated with nattokinase. A natural component of the soy food natto, nattokinase has been part of the Japanese diet for hundreds of years. For 30 years nattokinase has been used as a natural medicine in concentrations (i.e., doses) similar to those consumed in food with no side effects or adverse reactions. Do not combine nattokinase with drug blood thinners—e.g., aspirin, Coumadin (warfarin), or heparin. Patients taking blood thinners should consult their alternative health care practitioner before taking nattokinase. Pregnant women, breast-feeding mothers, and people with bleeding disorders should not take nattokinase. As with other anticoagulants, discontinue two weeks before scheduled surgery.



*Natto*

If you choose just one nutritional medicine to lower your fibrinogen, make it nattokinase.

Don't worry if your nattokinase doesn't cause your fibrinogen level to go down.

Nattokinase does not block fibrinogen production; instead, it dissolves the solid fibrin strands formed from soluble fibrinogen, so it won't always lower fibrinogen levels, but it will still be protecting you from excess fibrinogen.

**Dose**

Take 1-2 100 mg capsules twice daily.



*Turmeric, the herb from which curcumin is derived.*

## Curcumin (a component of the herb turmeric)

Curcumin (*curcumin longa*) is the bright orange-colored active ingredient in the popular native Indonesian and South Indian spice, turmeric. Think curry here. Curcumin contains potent antioxidant and anti-inflammatory compounds that block hepatic fibrinogen production.

Curcumin also addresses and reverses several other molecular biological changes that set the stage for stroke, heart attack, and hypertension.

Curcumin also protects against the adverse effects of too much fibrinogen by blocking “platelet aggregation.” (Platelets, the blood clotting cells, normally float freely in the bloodstream, but right before a clot forms, they start hanging out in clumps—or aggregates.)

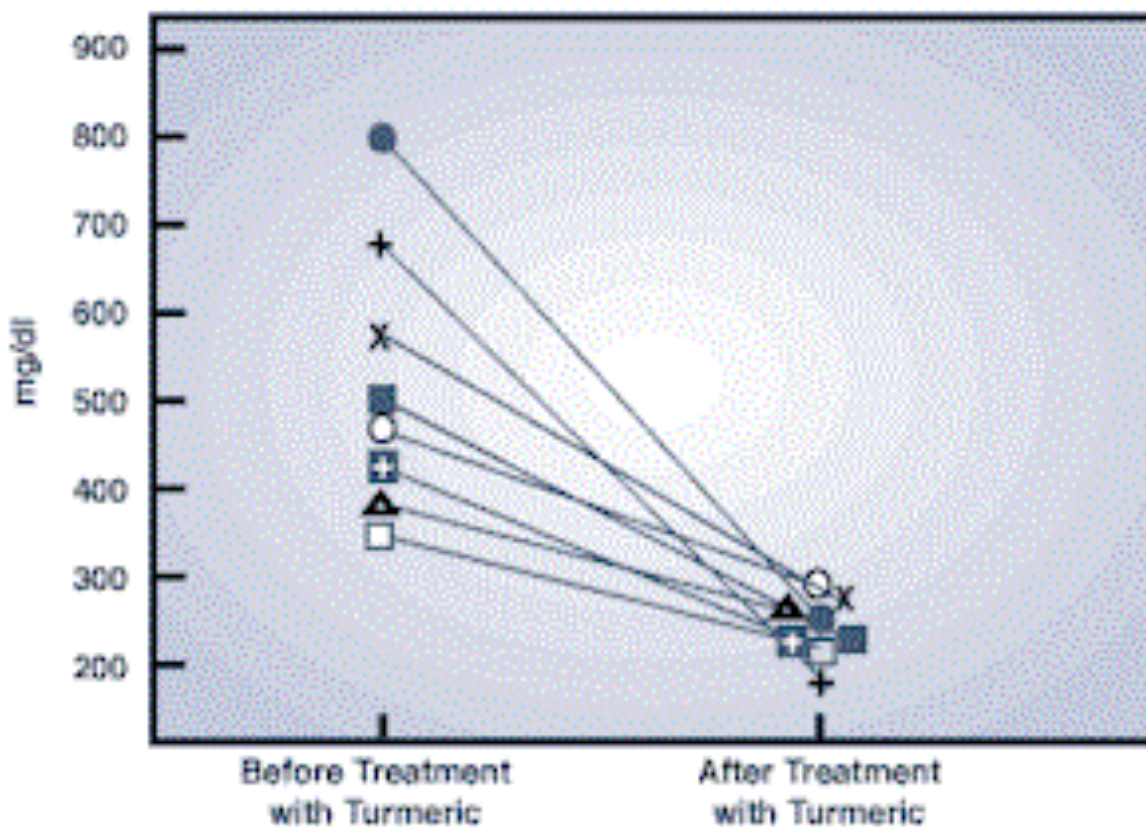


Fig. 4: Effects of Turmeric on plasma fibrinogen levels in eight subjects after only 15 days treatment (Ramirez-Bosca, 2000).

*Curcumin lowers fibrinogen levels.*

### Curcumin addresses virtually every aspect of atherosclerosis

An elevated fibrinogen level (over 250 mg/dL) represents the tip of a large and complex iceberg of molecular responses and interconnected vascular changes, most of which, amazingly, are addressed by curcumin. Allow me to try to describe the complex set of events addressed by

curcumin. By the time fibrinogen has become elevated, the inflammatory response is in full swing, and the stage is set for a stroke or a heart attack. Pro-inflammatory biochemicals like fibrinogen are being manufactured and released by the liver and endothelium and have flooded the system. The blood is thicker and more likely to clot. Platelets (our blood clotting cells) have been “activated”—that is, they are more likely to participate in the formation of a clot. Fibrinogen is ready to morph into fibrin and fibrin digesting enzymes have been deactivated so that fibrin is more likely to form. Vascular smooth muscle has now begun to proliferate and the arterial wall is thickening. LDL particles are being oxidized by the excess of free radicals generated by the inflammatory response. Oxidized LDL particles have launched a vicious and prolonged attack on the vascular endothelium and the media beneath it. While this attack is being waged, thrombi are very likely to form inside the vessel.

Mother Nature has conjured up a “dream herb” for reversing atherosclerosis and preventing heart attacks and strokes. Curcumin addresses every single one of the steps enumerated above. It reverses the inflammation, heals the damaged endothelium, thins the blood, reverses platelet activation, prevents oxidation of LDL, and blocks thrombus formation.

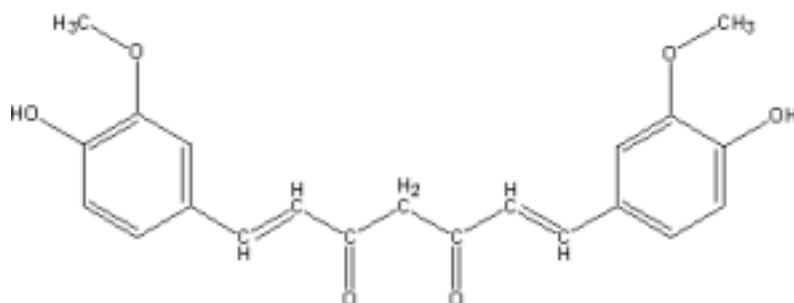
### **Broad spectrum cardiovascular effects**

Researchers have shown that curcumin exerts the following vascular effects:

- reduces C-reactive protein (CRP) levels
- prevents oxidation of LDL (oxidized LDL inflicts damage to the arterial wall causing atherosclerosis)
- increases HDL-cholesterol (HDL removes cholesterol from atherosclerotic arteries and returns it to the liver for removal; high levels of HDL protect against atherosclerosis.)
- reverses the endothelial dysfunction caused by high glucose levels (seen in patients with insulin resistance and TMS)
- blocks initiation and progression of atherosclerosis
- strengthens and protects the cardiovascular system
- reverses the vascular dysfunction caused by oxidative stress
- anti-thrombotic—i.e., prevents abnormal platelet aggregation, thus reducing the probability of clot formation
- blocks overstimulation of the inflammatory response that accelerates cardiovascular disease
- inhibits proliferation of vascular smooth muscle cells (this blocks the increased arterial wall thickness associated with cardiovascular aging and arteriosclerosis)
- reduces systemic inflammation by inhibiting inflammation-stimulating transcription factor NF-kappa B, the inflammatory enzymes COX-2 and 5-LOX, and cytokines, including interleukin 6 and TNF (tumor necrosis factor)
- inhibits fat cell (adipocyte) derived inflammatory mediators. (Adipocytes generate chronic low-grade inflammation that leads to cardiovascular disease and to insulin resistance.)



*Curcumin*



*Molecular structure of curcumin.*

### **An anti-aging, optimum health bonanza**

Beyond its vascular effects, curcumin displays a remarkable array of healthful, curative, even life-extending properties. Hundreds of research studies have documented the following medicinal and anti-aging effects:

- anti-cancer
- anti-arthritic
- anti-inflammatory
- pain-reducing
- antiedemic (reverses water retention)
- anti-tumor
- anti-mutagenic
- hepatoprotective
- antihypercholesterolemic (lowers cholesterol)
- nephrotonic (good for the kidneys)
- antihypertensive
- chemoprotective
- carminative (anti-gas)
- anti-HIV

- anti-herpes simplex virus 1 and 2
- anti-malarial
- antimicrobial
- anti-parasitic

### **Osteoarthritis (and other inflammatory) pain relief**

In a study of 107 patients suffering from osteoarthritis of the knee, two grams of curcumin extract daily for six weeks achieved slightly better pain reduction scores than subjects given 800 mg of ibuprofen. Over 90% of the curcumin patients reported satisfaction, as compared to 80 % for the ibuprofen users.

### **Good for brain chemistry**

Several recent studies examining brain neurochemistry and cognitive functioning showed that curcumin increased levels of the mood-related neurotransmitters serotonin and dopamine. The herb also was found to enhance the effectiveness of antidepressant drugs by inhibiting levels of the enzyme monoamine oxidase. Animal studies have shown that curcumin reduces levels of the stress hormone corticosterone, reverses chronic stress-induced cognitive dysfunction, and improves memory.

### **Dose and delivery**

2-8 500 mg capsules twice daily, or use turmeric liberally in cooking. 2-8 grams a day have been used in research studies. Curcumin is not well-absorbed. Purchase only “phytosome” products in which curcumin has been bonded to a fat soluble substrate like phosphatidylcholine to enhance absorption.

## **Serrapeptase**

Serrapeptase (serrapeptidase, Serratia peptidase), a proteolytic (protein-digesting) enzyme, is an anti-inflammatory nutritional medicine that dissolves plaque, and removes both fibrin and fibrinogen by digesting them. Serrapeptase also selectively removes many other proteins that impede healing and optimum health.

With a long history of safe and effective use in Asia and Europe, serrapeptase has established itself as a reliable treatment for virtually all disorders in which pain, infection, and/or inflammation are prominent features. It is free of side effects or adverse reactions.

Serrapeptase seems almost too good to be true. How can one natural medicine dissolve arterial plaque, digest away blood clots (including thrombi), prevent atherosclerosis, alleviate arthritic and neuropathic pain, reverse inflammation, reduce edema (swelling and fluid retention), speed up healing and tissue repair, and remove scar tissue? The key to understanding how Serrapeptase could have such a broad spectrum of activity is that, as a proteolytic enzyme, it digests away unwanted proteins; it selectively digests away non-living tissue without harming living tissue. These properties address the essence of healing and regeneration of damaged tissue. Serrapeptase somehow “knows” the difference between necessary proteins (which comprise many of the most important structures in our bodies) and proteins that are unnecessary and unwanted (such as fibrinogen, fibrin, blood clots, atherosclerotic plaque, unwanted mucus, proteins that cause arthritic swelling and pain, other inflammatory proteins, and even scar tissue). Serrapeptase selectively removes the unwanted proteins, leaving all essential structures intact.



Serrapeptase was originally discovered centuries ago by Chinese Traditional Medicine herbalists. Technically known as Serratia peptidase, serrapeptase is produced by *Serratia mercesans*, a bacterium that populates the silkworm's digestive system. The enzyme is regurgitated by the moth when, after metamorphosis, it is ready to digest its way out of its cocoon—which happens to be made of an “unwanted” protein: silk!

### **Vascular system**

At its core, atherosclerosis is an inflammatory condition in which endothelial irritants (see list in Chapter 5) trigger an inflammatory response in the arterial wall. Serrapeptase digests away the irritating proteins, thus reducing local inflammation. Serrapeptase outshines anticoagulant and anti-inflammatory drugs in that it dissolves the fibrin deposits and related inflammatory proteins that would otherwise become vessel-blocking plaque and thrombi. No drug can do that.

### **Anti-inflammatory, blocks pain, non-toxic alternative to pain-relievers**

Because it can prevent the release of pain-inducing amines (such as bradykinin) from inflamed tissues, Serrapeptase relieves pain in a wide assortment of conditions, including osteoarthritis, rheumatoid arthritis, trauma, back pain, cervical pain, bursitis, muscle spasm, bone spurs, headaches, neuropathy, post-surgical pain, and just about any other disorder that involves inflamed and painful muscles, nerves, ligaments, and tendons. Physicians throughout Europe and Asia use serrapeptase as a harmless, side effect-free alternative to toxic drugs such as ibuprofen, salicylates, and other NSAIDs.

### **Promotes respiratory and sinus health**

By digesting away the excess mucus secretions and scar tissue that block airways and lead to infection, serrapeptase has been successfully applied in a variety of respiratory conditions including asthma, rhinitis, sinusitis, otitis, chronic bronchitis, bronchiectasis, emphysema, chronic obstructive pulmonary disease (COPD), and cystic fibrosis.

### **Accelerated tissue repair**

Healing from injuries, infections, and inflammatory disease is slowed by swelling and fluid retention. Serrapeptase speeds up healing by removing scar tissue and unwanted inflammatory proteins, and by facilitating fluid drainage.

### **Post-operative pain**

One double-blind study examined the effect of serrapeptase on post-operative swelling and pain in 66 patients who had just received surgery for repair of a ruptured lateral collateral knee ligament. On the third post-operative day, the group receiving serrapeptase exhibited 50 percent less swelling and significantly lower pain levels than controls.

### **Anti-microbial effect; digests biofilm; potentiates antibiotics; speeds healing from infections**

Serrapeptase blocks the ability of pathogenic microorganisms to generate biofilm, the microbial secretions that form a protective wall around bacterial and fungal colonies. Serrapeptase digests this biofilm barrier, allowing immune cells and antibiotics to move in for the kill.

### **An alternative to NSAID drug toxicity**

The July 1998 issue of The American Journal of Medicine discussed NSAID-related gastrointestinal and metabolic complications: “Conservative calculations estimate that approximately 107,000 patients are hospitalized annually for non-steroidal anti-inflammatory drug (NSAID)-related gastrointestinal (GI) complications and at least 16,500 NSAID-related deaths occur each year among arthritis patients alone. The figures of all NSAID users would be overwhelming, yet the scope of this problem is generally under-appreciated.”

### **Dose**

The usual recommended dose is 2-6 enteric-coated capsules once or twice daily on an empty stomach. (This is important because serrapeptase will digest the protein in food rather than being absorbed intact.) The total dose of serrapeptase per day is between 10 and 30 mg on an empty stomach preferably in three divided doses.

### **Enteric coated**

Be sure the serrapeptase product you choose comes with a pH resistant enteric coating to ensure protection from stomach acid, allowing disintegration only after entering the alkaline environment of the small intestine. This increases small intestinal absorption, thus enhancing systemic activity and efficacy.

### **Product quality**

Products vary in quality and potency. Some companies marketing deceptively-named serrapeptase knockoff products that they claim are comparable or equally effective. When considering these products and claims, keep in mind that the published research was done on serrapeptase, not the wannabes.

### **Precautions**

Do not use with blood thinners. Systemic proteases like serrapeptase have antithrombotic properties and may therefore increase clotting times in persons taking Coumadin (warfarin), aspirin, and Plavix. Patients taking antibiotics should consult a physician before taking Serrapeptase as it may improve vascular permeability, thus increasing the rate of antibiotic absorption and delivery.

## **Flaxseed oil**

An essential nutrient (like a vitamin, but oily) flaxseed oil (FSO) is a broad-spectrum anti-inflammatory agent that serves up a bonanza of heart-healthy effects: beyond strengthening the cells of the vascular wall, FSO lowers C-reactive protein, cholesterol, LDL, and fibrinogen.

FSO also lowers levels of clot-promoting thromboxanes, a family of compounds found in blood platelets (blood clotting cells). Thromboxanes encourage platelets and red blood cells to stick together, forming a clot—that’s *blood clot*, as in heart attack or stroke. Researchers report that the alpha-linolenic acid in flaxseed oil markedly lowers the biosynthesis of unfavorable thromboxanes and fibrinogen, thus inhibiting the platelet aggregation and excessive thromboxane activity that accelerate clot formation.

**Dose**

1 tablespoon or 6-8 capsules daily.

## **Bromelain**

This proteolytic (protein-digesting) enzyme derived from pineapple stems is one of the most effective fibrinogen-lowering agents. Bromelain (*Ananas comosus*) activates plasmin, our bodies' own enzyme for lowering fibrinogen levels. Activated plasmin digests both fibrinogen and fibrin.

Bromelain is a blood thinner. Therefore, individuals taking warfarin, Coumadin or other prescription blood thinners should discuss bromelain with their alternative health care practitioner before deciding to take it.

**Dose**

2-6 250 mg capsules two or three times daily, taken away from meals if possible).

## **Green Tea**

Rich in flavonoid catechin polyphenol antioxidants such as EGCG (epigallocatechin gallate), green tea lowers fibrinogen levels and protects against cardiovascular disease. Research and 25 years of clinical use in Europe and Asia has demonstrated that green tea reduces the risk of cancer, osteoarthritis, impaired immune function, infection, gum disease, and even tooth decay.

EGCG, the main active component in green tea leaves, protects your cells from oxidative damage by those nasty omnipresent free radicals that can shorten your life by causing cancer, arteriosclerosis, heart disease and accelerated aging. EGCG inhibits oxidation of fats (including the all-important LDL particle), and assists in weight loss. The polyphenols in green tea improve blood sugar regulation in persons with insulin resistance, lower cholesterol, and block the development of the clots (called anti-thrombotic activity) that lead to heart attacks and strokes. EGCG and other green tea phenols also protect our DNA from ultraviolet and visible radiation-induced damage: at least one researcher has shown that sipping green tea before exposure decreases sunburn. Black tea leaves contain a little EGCG but much less than the green alternative.

**Dose**

2-4 capsules green tea extract (500 mg each providing 250 mg of catechins and polyphenols) once or twice daily, or 2-8 cups per day of organic green tea.

## **Diet to lower fibrinogen**

**Low carb diet**

See Chapter 11: Blood Sugar, Insulin Resistance, and The Metabolic Syndrome.

**Indian Curries**

Whip yourself up a tasty curry dish pleasantly seasoned with lots of turmeric (curcumin; curry powder), olive oil, garlic, onions, shallots and ginger. Every single one of these ingredients will contribute to a reduction of your fibrinogen level.

### **Olive oil**

Shown to lower fibrinogen in humans with elevated fibrinogen levels. Use olive oil in salad dressings and for cooking as your principal source of dietary fat.

### **Garlic**

Two to four capsules once or twice daily, or cook using fresh cloves.

### **Ginger**

An anti-inflammatory herb. Better than aspirin at blocking clots. Like aspirin, ginger exerts its anticoagulant effect by inhibiting the enzyme COX-1 (which increases platelet stickiness in preparation for clot formation).

Whenever possible, cook with these fibrinogen lowering foods: garlic, ginger, onions, shallots, rosemary, and turmeric (curcumin).

### **Green tea**

Organic green (not black) tea contains numerous compounds shown to prevent and reverse damage to the cardiovascular system. In Asia, it is not unusual to drink 8-10 cups a day. (See description of green tea in supplement section above.)

### **Mediterranean Diet**

The traditional cooking style of countries bordering the Mediterranean Sea, this diet has been shown in numerous large-scale studies to be associated with significantly low risk of cardiovascular disease. The Mediterranean Diet specifically lowers fibrinogen. The key components of a Mediterranean Diet include:

- Generous amounts of *fruit and vegetables*
- Healthy fats, especially *olive oil*
- *Nuts*, especially walnuts
- *Red wine* in moderation
- *No* (or very small amounts of very lean) *meat*.
- The diet specifically *discourages saturated fats* (found in meat and dairy but not in plant products) *and hydrogenated oils* (AKA “funny fats” or *trans-fats*).

## **Fibrinogen-lowering Lifestyle**

- **Daily exercise** will significantly reduce elevated fibrinogen levels.
- **Weight loss** - Fibrinogen-driven hyper-coagulation is associated with obesity. Losing weight lowers the fibrinogen.
- **Lower your homocysteine** if high (>7.0). Elevated homocysteine levels inhibit tissue plasminogen activator (TPA), which blocks the body’s natural breakdown of the fibrin generated from fibrinogen. So a high homocysteine causes fibrinogen to go up. See Chapter 9.
- **Quit smoking**. Smoking increases fibrinogen levels; quitting lowers them.

## Additional fibrinogen-lowering nutritional medicines

- **DHEA** suppresses interleukin-6 and other dangerous proinflammatory cytokines produced in the liver that trigger fibrinogen production. Follow-up testing is necessary to ensure optimum dose. For more about DHEA, see chapter 33 in my book, *Renewal: The Anti-Aging Revolution* (Rodale 1998; St. Martin's Press 1999). Dose should be determined by testing. Optimum range is 300-500 mcg/dL for women; 500-800 mcg/dL for men.
- **Policosanol** Marketed primarily as a natural cholesterol lowering agent, policosanol has also been shown to lower fibrinogen levels by inhibiting platelet aggregation and blocking a clotting factor known as thromboxane. In animal studies, policosanol reduced the size of experimentally induced thromboses. Dose: 20-40 mg per day.
- **Natural estrogen replacement therapy** predictably lowers fibrinogen levels in perimenopausal and postmenopausal women. Be sure to use *natural* estrogen and balance it with natural progesterone. Not recommended for women with a personal or family history of breast, uterine, or ovarian cancers. Follow-up testing is necessary to ensure optimum dose. See chapters 32 and 35 of my book, *Renewal: The Anti-Aging Revolution*.
- **Ginkgo biloba** Ginkgo's many vascular benefits are discussed in chapter 27 of *Renewal: The Anti-Aging Revolution*. Dose: 120-240 mg daily.
- **Vitamin A and beta-carotene**
- **Vitamin C** has been shown to reverse fibrinogen's clot enhancing effects., which it accomplishes by breaking up the clumping and clots caused by excess fibrinogen. In a report published in the journal *Atherosclerosis*, heart disease patients given 2,000 mg a day of vitamin C experienced a 27 percent decrease in the platelet aggregation index (PAI, a measure of propensity to clotting), a 12 percent reduction in total cholesterol, and a 45 percent increase in fibrinolytic (clot-busting) activity.
- **Vitamin E** doesn't lower fibrinogen but does inhibit clotting by blocking platelet aggregation. "Mixed tocopherols" more effectively inhibit platelet aggregation than alpha-tocopherol alone.
- **Vitamin K** suppresses the pro-inflammatory cytokine interleukin-6.
- **Niacin** (a B-complex vitamin)
- **Pantethine** (pantothenic acid, a B-complex vitamin)
- **Licorice** (glycerrhizin) extract inhibits the clotting agent thrombin.
- **IP-6** (inositol hexaphosphate). Primarily known as a potent immune booster and anti-cancer nutrient, IP-6 also inhibits platelet aggregation and platelet stickiness, both of which enhance fibrinogen's clot-promoting activity.

## Drugs that lower fibrinogen

No FDA-approved drug will lower your fibrinogen level.

The popular cholesterol-lowering drug Lopid (gemfibrozil) actually *increases* fibrinogen levels by 10 to 20%!

Coumadin (warfarin) reduces the risk of clots in the short run, but is a toxic drug with multiple adverse effects, including hemorrhage, necrosis, and osteoporosis. Nattokinase is

preferable because it reduces coagulation gently and naturally, and because (unlike Coumadin) it dissolves clots and thrombi that have already formed.

## *Chapter 11*

# **Blood Sugar, Insulin Resistance, and The Metabolic Syndrome**

### **“Please calm down, Mr. Shoemaker.”**

*Dave Shoemaker, a fifty year old English professor at a small private college, had worked hard, played hard, loved his wife, his job, his friends, his life. He didn't want his world to change.*

*A football fanatic, Dave kept a San Francisco 49ers helmet signed by Joe Montana in a glass case in his study. He loved to cook, and his wife loved him for it. Together they had many friends, and an active social life. Old hippies, they regularly attended rock concerts. Deeply committed to his two teenagers, Dave stayed involved in their lives, driving them (and often whole teams) to volleyball and soccer games, donating most weekends while putting other important areas of his life on hold.*

*Three years ago Dr. Oakes, Dave's family physician, discovered that his blood pressure was “a little high, nothing to worry about, nothing we don't expect at your age.” Noting that Dave's dad and uncle had both died of heart attacks, Dr. Oakes prescribed a diuretic to keep the blood pressure down.*

*Dave carried a bit of a pot belly (we call this “central adiposity”), so Dr. Oakes also suggested a weight loss program. Having followed his doctor's orders for blood pressure and weight loss, Dave felt he was “home free” and needn't fear a heart attack. Nothing could have been further from the truth.*

*One cool spring evening after his typical low fat dinner, Dave's good life came to a screeching halt. He had been helping his 18-year-old, Mandy, with her homework, and, “Out of the blue I have this tight, crushing feeling, like an elephant standing on my chest,” he told the ER doctor. “I can't get my breath. Millie drove me here. What's wrong?”*

*The doc placed his hand reassuringly on Dave's right shoulder and in slow, even, comforting tones, said, “Mr. Shoemaker, you are having a myocardial infarction.”*

*“That's impossible! My blood pressure is fine, my cholesterol is normal, and I've been eating a low fat diet for a very long time. Okay, I'm a little overweight, but how could I be having a heart attack?”*

*“Please calm down, Mr. Shoemaker. It’s not good for your heart! We don’t know why, but about half of all heart attack patients are like you: their blood pressure and cholesterol are normal and they eat a low fat diet. Right now, we have to worry about stabilizing you. Later on, you can talk with your family doctor about why this happened, okay?”*

*Dave was admitted, and the next morning, when Dr. Oakes visited him on the ward, Dave posed the same questions.*

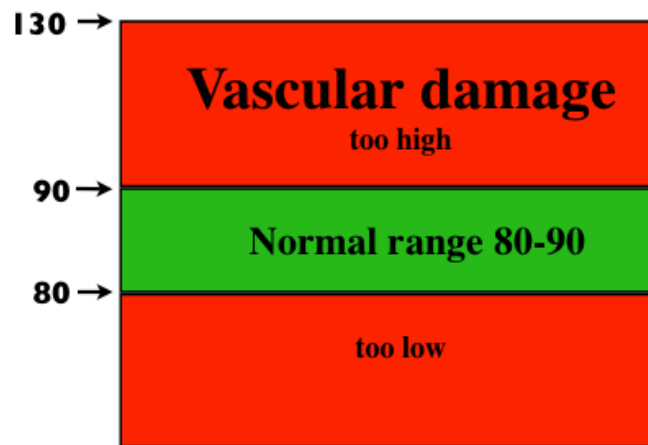
*“Dave,” he replied with a shrug, “we don’t know why simply lowering cholesterol and blood pressure isn’t curative for so many people. It’s true, you are doing everything right. It could be genetics; perhaps your family history is predisposing you to this. You just have to ‘learn to live with it.’” (I hate it when they say this because it’s never true.)*

*What neither Dave, nor Dr. Oakes, nor the ER doctor realized was that Dave suffered from a disease complex known as “the metabolic syndrome” (TMS).*

## Fasting Blood Sugar

**Prolonged elevation of glucose (as measured by fasting blood sugar) damages your blood vessels.**

**Prolonged  
fasting glucose  
above 90 mg/dL  
causes  
atherosclerosis**



healthy artery



atherosclerotic artery



atherosclerotic artery  
deadly thrombus

## The Metabolic Syndrome (TMS)

Gerald Reaven, Ph.D., of Stanford University was the first to recognize the metabolic syndrome. His research showed a statistical association between elevated blood sugar levels and four other markers: high triglycerides, low HDL, high blood pressure, and waistline expansion. Reaven originally assigned the name “Syndrome X” to this cluster of variables. Others have

referred to TMS as “dyslipidemic hypertension” or “insulin resistance syndrome.” Though catchy, the “Syndrome X” moniker has lost favor, gradually bowing to the more technically accurate “the metabolic syndrome.”

If you have **any three of the following five signs**, you have the metabolic syndrome:

- **a fasting blood sugar above 90**
- **extra fat around your middle (we call this “central adiposity”)**
- **a triglyceride level over 150**
- **HDL less than 40**
- **high blood pressure**

If you are over forty, a little overweight, have a slightly protruding abdomen (a pot belly, even a teeny one), and tend to be a couch potato, the likelihood is high that you have TMS.

One in four Americans has TMS. Most people over 50 have TMS. The risk conferred by TMS is so high that people who have it can be thought of as working on their first heart attack.

The first sign of TMS is usually a rise in fasting blood sugar levels above 90 mg/dL. (Fasting blood sugar can be measured alone, but is also a component of the standard “comprehensive metabolic panel.”)

Before Reaven’s research, we knew that extra blood sugar triggers a sequence of metabolic and hormonal events that ravage the endothelium. All by itself, a persistent elevated fasting blood sugar (FBS) was known to cause accelerated atherosclerosis. But Reaven was the first to show that the already high risk of heart attack conferred by an elevated FBS becomes exponentially higher if the individual also has at least two of the remaining four factors (a “spare tire”—even a tiny one, high triglycerides, low HDL, and/or high blood pressure).

## **Insulin resistance**

An elevated fasting blood sugar (and/or TMS) tells us that this patient has lost the ability to manage blood sugar. More specifically, he or she has developed a condition known as “insulin resistance,” a metabolic disorder in which insulin receptors have stopped responding to insulin.

Here’s how insulin resistance works. We need energy to drive the many chemical reactions of life and we get that energy by burning fuel (the sugar glucose) in oxygen (supplied by the lungs). We need a constant and evenly released supply of glucose. Too much or too little causes problems. The blood sugar regulating system I am about to describe makes sure the burning process is steady.

As food is absorbed after every meal, blood sugar levels rise. Your pancreas monitors blood sugar and, when it detects that rise, it secretes extra insulin into the bloodstream. When insulin arrives at the outer surface of liver and muscle cells, it attaches to insulin receptors there and sends a command telling that cell to remove excess sugar from the bloodstream and store it as glycogen for use later on. This system, when healthy, works to keep blood sugar steady.

With insulin resistance the insulin receptors have grown weary and begin to respond sluggishly to the insulin messages. The receptors appear to be “resisting” the insulin messages. When insulin resistance sets in, the muscle and liver cells remove less sugar from the bloodstream, and—since less sugar is being removed—this causes a rise in fasting blood sugar (FBS). When FBS reaches 90 mg/dL or more, we know that insulin receptors are damaged and malfunctioning.



Soon the pancreas figures out that its insulin messages aren't being heard, so it tries to fix the situation by ratcheting up insulin production. People with insulin resistance and the metabolic syndrome therefore typically have high levels of insulin in the blood ("hyperinsulinemia").

Though doctors may use a variety of terms to describe insulin resistance, including "blood sugar dysregulation," "elevated blood sugar," and "pre-diabetes," the underlying cause is always the same: loss of control over blood sugar because of damage to insulin receptors.

Insulin resistance does not happen in a vacuum; it's usually accompanied by a pattern of other signs indicating the presence of the metabolic dysfunction. The diagnosis of TMS is an attempt to incorporate a diagnostic recognition of these additional changes. As mentioned above, when insulin resistance occurs (as manifested by blood sugar > 90), it is often accompanied by four related metabolic phenomena: rising triglycerides, lower HDL level, elevated blood pressure and abdominal fat accumulation (pot belly). When doctors see these signs, they will (hopefully) recognize and treat TMS.

The diagnosis of TMS requires *at least three* of the following five signs:

- Elevated **fasting blood sugar** (over 90 mg/dL)
- Elevated **triglycerides (TGs)** (>150 mg/dL)
- Low **HDL** (<40)
- Elevated **blood pressure** (>140/>85)
- "**Central adiposity.**" (extra fat around the middle) - males with more than a 34 inches waistline or females with over 40 inches

## **As we get older TMS will affect most of us**

TMS is not a rare disorder: 75 million Americans suffer from it. Like Dave, very few know they have it. Dave's blood sugar had crept up to well over 100 (as you know, anything over 90 is too much). His triglycerides (TG) were over 200 (up to 150 is okay) and his HDL (the "good" cholesterol) had dropped below 35 (should be > 40). These three markers, plus central adiposity (fat around the middle) and elevated blood pressure constitute the five cardinal signs of TMS. Dave had them all.

Dave came home from the hospital with more drugs. His TMS, however, went undiagnosed. No one told him to exercise. No one told him he had to cut way back on carbs. No one explained how to use nutritional supplements to reverse his insulin resistance. After three months on this "program," Dave suffered a second massive coronary occlusion. This time he almost died. Again, the doctors failed to make the correct diagnosis. Dave began wondering whether his treatment plan was working, and a friend referred him to me. The diagnosis of TMS was simple because he had all of the symptoms and signs of it. Once we got him going on a program for TMS (see below), he started improving.

## **Why should I care if my blood sugar is elevated?**

TMS is never accompanied by any discomforting symptoms, so why would one care whether it's happening? In a word (okay, two words): *accelerated atherosclerosis*. Persistent blood sugar elevations damage arteries, cause plaque deposition, and accelerate the atherosclerotic changes that lead to strokes and heart attacks.

Many doctors dismiss minor elevations of fasting blood sugar. If your doctor does this, have a long talk (good luck with that; most doctors are too busy!), then show him or her this

book, and if you still get resistance, it may be time to move on. Like Dave, you need a physician who understands the metabolic syndrome and knows how to treat it aggressively.

## How can I tell whether I have TMS? The five cardinal signs of The Metabolic Syndrome

Other than a pudgy waistline (and this might not even be present), there may be no outward signs of TMS. As I have emphasized throughout this book, to detect risk one must do the biomarker testing and know the numbers.



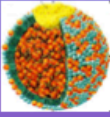


Every year thousands of patients die because their physicians ignore the signs of TMS while overestimating the relative importance of lowering cholesterol.

If you have *any three* of the following five signs, you have the metabolic syndrome: extra fat around your middle, a fasting blood sugar above 90, triglyceride level over 150, HDL less than 40, high blood pressure.

**Elevated blood sugar** is closely associated with another common disease called:

### *The Metabolic Syndrome*

which consists of:

- **High fasting blood sugar (>90)** 
- **Elevated triglycerides** above 150 mg/dL 
- **Low HDL** below 40 mg/dL 
- **High blood pressure:** above 130/85 (without blood pressure lowering drugs). 
- **Central adiposity (“pot belly”)** (waistline > 34 inches for men)  
Abdominal fat (technically known as “central adiposity”). That spare tire or bulging belly makes you a prime candidate for The Metabolic Syndrome. Count yourself in if you are a male with more than 34 inches around the middle, or a female whose waistline is greater than 40 inches. 

Other risk markers often (but not always) found in conjunction with the metabolic syndrome include:

- Abnormal LDL particle size profile featuring Type B (“bad”) small dense LDL particles (see Chapter 7).
- Elevated fibrinogen level (see Chapter 10).
- Elevated C-reactive protein (see Chapter 8).

Poor diet, stress, smoking, alcohol consumption, and sedentary lifestyle increase risk for developing TMS.

## **The “disease of the new millennium”**

The convergence of markers for TMS is far more ominous than an elevation of any individual heart marker, so doctors who understand cardiovascular disease take it very seriously.

Men and women with TMS constitute the group at greatest risk of death from heart attack. In fact, studies have shown that the risk of heart attack, heart disease, and stroke is nearly three times higher in people with the metabolic syndrome. According to Dr. Steven Nissen, distinguished Cleveland Clinic cardiologist, “This is the disease of the new millennium.”

The Centers for Disease Control (CDC) tells us that one in four adults in the U.S. (about 75 million individuals) has signs of metabolic syndrome and will most likely die from it.

The numbers are expected to grow because of Americans’ sedentary lifestyle. A study of 1,209 men aged 42 to 60, over a 15-year period, found that those with metabolic syndrome were from 2.9 to 4.2 times more likely to die of a heart attack than those who did not have the condition.

"I see now, patients in their 20s and 30s with the metabolic syndrome and this does not bode well for their risk of heart attack and stroke when they [reach] 40 or 50 years of age," says Richard Nesto, M.D., Associate Professor of Medicine, Harvard Medical School, and Chairman of the Department of Cardiovascular Medicine at Lahey Clinic (a teaching hospital of Tufts University).

"The metabolic syndrome has been there for a while," says Dr. Nesto. "We just have not recognized its importance. I think doctors in the past have looked at patients without looking at the big picture," he said. "They've looked at risk factors in isolation and treated them one by one. Now we should look at patients as to whether they have the metabolic syndrome."

If one examines the individual risk factors separately, they don't seem all that bad. When taken together, however, you end up with a skyrocketing atherogenic potential that is far greater than just the sum of the parts. Doctors can no longer afford to isolate and treat individual risk factors such as cholesterol or hypertension. This was the approach Dave Shoemaker received, and it produced a disaster.

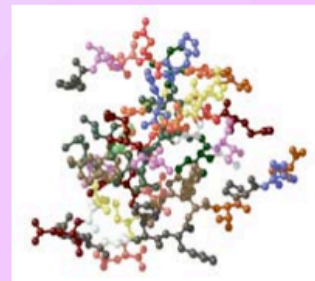
# What causes blood sugar to go up?

*Elevated blood sugar is caused by a phenomenon called “**Insulin Resistance.**”*

**Insulin** is a hormone released by the pancreas that **stimulates insulin receptors** in liver and muscle cells, telling them to remove sugar from the bloodstream.

**Insulin resistance occurs when insulin receptors fail to respond** to the insulin hormonal messages.

When insulin receptors malfunction, glucose can no longer be taken up by the liver and muscle cells, so it stays in the bloodstream, causing **elevated blood sugar.**



an insulin molecule

*Insulin receptor failure causes blood sugar to rise.*

## Insulin resistance: the driving force behind TMS

Okay, now you know what to look for—and why it’s important. You already know that the main causative factor for the metabolic syndrome is insulin resistance, caused when insulin receptors fail and blood sugar climbs. Now I am going to take you a little deeper into the biochemistry and molecular biology of it.

Let’s start with how blood sugar is regulated in a healthy body. The food we ingest contains carbohydrates which are digested down into sugars that are then absorbed into the bloodstream. These absorbed sugars raise our blood sugar (glucose) level. Our pancreas detects this rise in blood sugar, and secretes a little extra insulin, which travels through the bloodstream to the liver and muscles. There it attaches to insulin receptors on the surface of liver and muscle cells, telling them to remove some of the sugar from the bloodstream (to be stored as glycogen for later use). Removal of some sugar lowers the blood sugar level, so the pancreas decreases its insulin production.

There’s a feedback loop here. The liver and muscles are continuously “listening” to the insulin “messages” sent from the pancreas, and removing more sugar if the “volume” goes up. The pancreas is likewise “listening” to the blood sugar level; it increases insulin production when the sugar goes up and decreases it when sugar goes down.

Now imagine what would happen if the insulin receptors in the liver and muscles began turning a deaf ear to the insulin. First you’d have less sugar being pulled out of the bloodstream

and stored as glycogen. Then blood sugar levels would rise. The pancreas would notice this and compensate by releasing more insulin. That insulin would not be completely effective at clearing the extra sugar, so the pancreas would work harder to make and more insulin, but less and less of the sugar would be removed, so the blood sugar would creep higher. Once it's consistently above 90, insulin resistance is born—and along with it, accelerated atherosclerosis.

If insulin receptor failure persists, the blood sugar can go even higher. If it reaches 115, we now have full-blown type 2 diabetes, but more often it hangs out in the 90-110 range—clear-cut TMS. Either way, there is a problem.

Why do insulin receptors fail? We don't know, but we do know that its appearance is almost always accompanied by some combination of excess carbohydrate consumption, insufficient exercise, aging (it's way less likely in people under 40), and genetic predisposition.

TMS develops slowly, and a decade or so may pass during which slight abnormalities in blood sugar, blood pressure, triglycerides, abdominal fat and HDL go unnoticed. Watch for this “upward creep,” and if your belly is bulging a little or your blood pressure is higher than it had been, get tested. If your triglycerides and blood sugar are slipping upwards or your HDL downwards—even though they may still be in the normal range—this is probably TMS in the making. Diagnosing your own TMS and reversing it in the earliest stages is far preferable to waiting until a doctor diagnoses it in the advanced stages.

## Insulin Resistance

In **young** people, insulin receptors work fine, even with high dietary carbohydrate intake.

However, many **older** adults lose the ability to process high carb loads. The same **high carb diet** that was easily tolerated in youth now **damages insulin receptors** and drives up blood sugar, causing fat deposition, weight gain, lipid changes, high blood pressure, and atherosclerosis.



example of a high carb load

- **Not rare:** 75 million (one in four) Americans suffers from insulin resistance.
- **Silent:** very few know they have it because *there are no symptoms.*

## Most people can reverse TMS by lowering carb consumption and exercising every day

It is important to know that you have control over your TMS; you can reverse it. There are three main causes of TMS: sedentary lifestyle, high carb diet, and aging. There isn't much any of

us can do about getting older, but you can exercise every day, and you can choose to eat a low carb diet. That's enough to normalize blood sugar in most individuals.

We live in the midst of an epidemic of excess carb intake that causes insulin overload that, in turn, causes obesity. Eating too many carbohydrates has some very undesirable consequences. First, our pancreas secretes excess insulin in an attempt to remove the extra sugar from the bloodstream and store it (as glycogen) in the liver and muscles. When the liver and muscle stores are full (it doesn't take much), the body still has to do something with remaining blood sugar, so guess where it goes? It's converted to fat and that fat is stored in the belly. The excess insulin that's stimulated by excess carbohydrates ends up promoting the accumulation of body fat. Therein lies a big (pun intended) problem: central adiposity, or fat around the middle. Lowering carb intake reverses this process, and reverses insulin resistance and TMS at the same time.

Exercise is the first line of treatment for metabolic syndrome because it influences all components of the disorder. Regular physical activity helps reduce excess body fat. Exercise improves insulin sensitivity. Exercise helps normalize blood pressure, as well, especially in people with borderline hypertension, the type of hypertension seen in metabolic syndrome. Exercise raises HDL cholesterol levels.

# How to Reverse Insulin Resistance and The Metabolic Syndrome

## Therapeutic Goals

- Lower fasting glucose to 90 mg/dL or less
- Lower elevated triglycerides to 150 mg/dL or less
- Raise HDL to 40 or greater
- Lower elevated blood pressure
- Lose weight if you are over your optimum

# **Lowering your fasting blood sugar and Reversing insulin resistance**

**Low carb diet**

**Exercise**

**Nutritional supplements**

- Cinnulin—2 capsules twice daily
- Glucose Control—2 capsules twice daily
- Alpha lipoic acid 100 mg.—3 tablets twice a day

## Recommended Program Overview

*Diet, exercise, and nutritional supplements* are the three pillars of therapy for the metabolic syndrome. When it comes to treating TMS, mainstream and alternative doctors agree that the starting point is *always* diet and exercise. Specifically, a *low carbohydrate diet* and *one hour of daily vigorous (i.e., aerobic) exercise* will usually correct insulin resistance and reverse the metabolic syndrome. (If you need to lose weight, make that one and a half hours daily.) Both components, diet and exercise, are absolutely necessary.

The addition of Cinnulin®, Glucose Control, and alpha lipoic acid will accelerate your progress by supporting the healing of insulin receptors.

Your program will need to address all components of TMS. So—if your triglycerides are elevated, your HDL low, your BP elevated, or waistline bulging—these must also be addressed as well. The diet and exercise prescription will go a long way toward correcting all of these. See recommendations below and in the corresponding chapters for additional advice.

## Low carb dieting

Experts agree that shifting to a low carbohydrate diet is essential for reversing insulin resistance and curing the metabolic syndrome. It's a common misconception that low carb dieting has to be painful.

Pay attention to carb levels in food types:

- **Veggies** are all zero (or very low) carbs, except root vegetables such as potatoes, beets and squashes which are 100% carb.
- **Meats** contain zero carbs.
- **Nuts, seeds, and beans**—at about 30% carb, 30% fat, and 30% protein—are by definition all low carb foods, so you can partake of these liberally without a need to combine.
- **Fruit**—especially berries—are a special case: technically high carb, but so nutritious that you can indulge in moderation without worry (see below).
- **Grains**—close to 100% carb content.



# A Low Carbohydrate Diet

## The rules:

In any meal, you can have some carbs, but *less than half* of total calories should come from carbs.

## Low carb foods

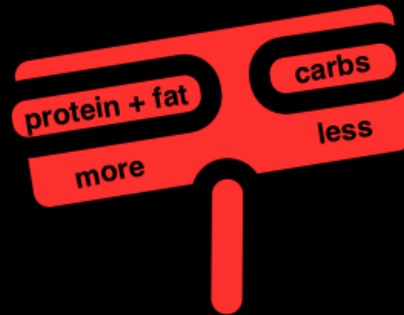
- all vegetables (except potatoes and squash)
- lean meat (chicken, turkey, beef, pork)
- eggs
- beans
- nuts
- fruit (contain some sugar, but are high in minerals, fiber, and phytochemicals; limit to three servings a day)

## High carb foods

- all breads and grains
- pasta and noodles
- cakes, cookies, pastries, baked goods
- starchy vegetables: potato, squash
- all sweetened foods and drinks
- candy
- crackers and most snack foods

## Low carb meals examples:

- toast with eggs
- bread with a salad
- rice with a stir fry or curry
- enchilada
- burrito
- salads
- beans (all)
- nuts (all)
- stir fries
- any egg dish
- all meats (small portions; low fat)



*Low carbohydrate diet rules, foods, and examples.*

## The Golden Rule of Low Carb Diets:

**Protein calories + Fat calories  $\geq$  Carb calories**

*In any and every meal, total calories from carbohydrates must be less than the sum of calories from fat plus protein.*

Keep in mind what I call “The Golden Rule of Low Carb Dieting.” In any given meal, **fat calories plus protein calories must be greater than carbohydrate calories.** Know carb food contents as listed above and read labels. Learn to quickly “eyeball” the carb content of a meal or snack. The “Golden Rule” makes it easy. Examples of low carb meals: eggs and toast, a chicken sandwich, salads, nuts with dried fruit, meat and vegetables. Just follow these simple guidelines:

- Load up on **veggies** (salads, steamed, stir-fired, baked); with the notable exception of root vegetables (potatoes, beets, carrots, and sweet potatoes) they are all low carb.

- **Beans, nuts, and seeds** are great for pumping up the protein side of the equation. These are all about 1/3 carb, 1/3 protein, 1/3 fat, so snacks nut, bean or seed snack is automatically a low carb snack.
- **Eggs** in any form are carb free and healthy as the Dickens.
- **Low fat meats** such as chicken and turkey breast, and lean ham are okay in modest quantities. The saturated fat found in fatty meat and dairy products causes atherosclerotic disease; stay away from it. Lean meats (for example, chicken without the skin, turkey breast, lean pork and beef), however, are very low in cholesterol. These are pure protein and won't cause a problem.
- **Fruit** (fresh or frozen) (in moderate quantities of 2-4 servings a day), even though they are technically higher carb foods, don't count toward total carbs because they contain so many incredibly nutritious phytonutrients and minerals. Sweetened juices and soda pop, however, are out. Blueberries, blackberries, raspberries, mango, cherries, and grapes contain extremely high concentrations of anti-heart disease, anti-cancer polyphenols and other beneficial phytonutrients. Eat lots of these fruit and balance the carbs in them with nuts and seeds, or soy milk.
- **Grains** (including wheat, rice, corn, cereals, pasta, breads and other baked goods) are 90%+ carbs. Minimize grains and make sure when you do eat them that you are following "The Golden Rule"—you can have them, but be sure to combine with enough fat and protein so that the carb portion is less than half.

## Low Carb Meal Ideas

- **salads (you can add nuts, seeds, beans, egg, meat)**
- **stir fries**
- **soups**
- **beans and bean dishes like chili**
- **steamed veggies**
- **tofu, soy milk, and all soy products**
- **chicken, turkey, beef, pork with salad and veggies**
- **eggs with ham, breakfast links, and fruit**
- **breakfast links (soy or pork) with toast**
- **sausage (chicken, soy, pork) and salad or steamed veggies**
- **omelets with vegetables, meat, cheese**
- **chicken, pork, or steak with onions, bell pepper, mushroom**
- **nuts (peanuts, almonds, walnuts, cashews, filberts, pecans)**
- **seeds (sunflower) as a snack or on salads**
- **Mediterranean diet**
- **Indian, Thai, or curries (hold the rice)**
- **Mexican (tacos, enchiladas, burritos) (no rice)**

•Remember: you can add small amounts of high carb foods to any of these.

*Low carbohydrate meal ideas.*

Read labels on packaged foods to determine carb content.

This may seem tedious at first, but once you get to know the carb content of your favorite foods, it will get quicker and easier.

**More ideas:**

- Egg (zero carb) with toast (high carb)
- Egg with ham (no carbs) or breakfast links (soy or pork).
- All the nuts (all kinds, including trail mix), seeds (sunflower) and beans you want.
- Add nuts and beans to otherwise high-carb meals to raise the protein+fat side of the equation.
- Lunch: soups and salads.
- Dinner: Stir fries, Mexican food (tacos, enchiladas, burritos, beans), salads, steamed veggies.
- All meat has zero carbs; so, you can combine meat with smaller amounts of carb foods like rice, corn, potatoes.
- Cereals (unsweetened, of course) are okay if you combine it with (unsweetened) soy milk and nuts or seeds to balance the carbs.

## Examples of **low carb salads:**

- **Greek** salad (put extra protein on, such as hard boiled eggs, chicken, or seafood)
- **Chicken** atop salad greens with any combination of chopped snow pea pods, chopped red pepper, and walnuts, cucumbers, pecans, or crumbled blue cheese
- **Cole slaw**
- **Tuna** salad with greens, tomato and avocado
- **Salmon** on top of greens, blanched green beans, mushrooms, and sprouts
- **Cobb** salad





# Daily aerobic exercise

- lowers blood sugar
- reverses insulin resistance
- reverses the metabolic syndrome
- heals damaged insulin receptors
- restores normal blood sugar control

*Benefits of exercise.*

## Exercise

It is impossible to reverse the metabolic syndrome without a daily exercise program: it's the *sine qua non* for success.

I am not talking here about climbing the stairs or parking your car and walking a few extra blocks to work (though not a bad idea). This exercise program consists of *daily one hour workouts* divided more or less equally between aerobic and strength components. If you need to lose weight, make that 1.5 hours.

If you have never been on an exercise program, enlist the services of a qualified trainer who can get you going on a custom-tailored program. It is *absolutely crucial* that you start out at a low level and *increase very gradually*. Having watched many patients initiate exercise programs in my 40 years of medical practice, I can tell you that it is an absolute *certainty* that you will suffer a potentially disabling injury if you increase your activity level too rapidly. *Go slow* at first and work up gradually!!! Your body needs time to get used to increased exercise, and if you push up your level too fast, you'll injure yourself. Going slow doesn't mean devoting less time; it just means going slower at first. Pain and excess fatigue are the two most common warning signs of over-exercising.

Most of us are so busy these days that we balk at the notion of yet another demand on our time. Can you afford an hour a day out of your already over stressed schedule? How important is it? Only you can answer these questions. But I would argue that finding the time—making it a priority—is an ultimately practical thing to do. Your investment in exercise time will pay huge dividends “down the road,” as it were—a stronger body and a longer and healthier life, devoid of the heart attack, stroke, hospitalization, debility, high health care costs, and a very much higher risk of premature death. Not to mention more time with the grandkids.

Why does exercise work? It improves our biochemistry and physiology in so many ways that I can only begin to explain it. Daily workouts widen and lengthen the freeway system of your blood vessels, and this enhances your body’s ability to deliver nutrients and fuel to all 100 trillion (or so) of your cells. By strengthening the heart muscle and building collateral vessels, exercise develops those alternate routes that come in real handy if one of the main freeways—like, perhaps a coronary artery—becomes blocked. Because “widened freeways” can remove waste material far more efficiently, conditioning is one of the most effective detox secrets around. In a physically fit individual, more blood (carrying more nutrients and oxygen) is delivered to even the most remote regions of your body. These are tissues that would otherwise be struggling and competing for supplies: the brain, liver, kidneys, immune system, sense organs, sex organs, endocrine glands—all start functioning better because they are no longer in a state of chronic semi-starvation.

Exercise addresses all five components of the metabolic syndrome: it reduces body fat, controls glucose levels by improving cellular insulin sensitivity and responsiveness, increases the ability of insulin receptors to bind with insulin and remove glucose from the blood, raises HDL levels, and normalizes blood pressure.

If exercise were available as a pill it would be the strongest known medicine—by a country mile.

## **Cinnulin® Cinnamon extract**

Dr. Richard A. Anderson and his colleagues at the Beltsville Human Nutrition Research Center of the U.S. Department of Agriculture screened extracts of 49 culinary and medicinal plants in a search for one that could mimic the effects of insulin, the hormone that regulates our blood sugar levels. They discovered that an extract of cinnamon acted like insulin in human cells. The active component in cinnamon responsible for its insulin-like activity is a water-soluble chemical compound called methylhydroxychalcone polymer (MHCP). They further found, to their amazement, that MHCP delivered insulin activity *identical to insulin*. In other words, insulin receptors were unable to distinguish the difference between MHCP and insulin. The cinnamon-derived compound did exactly what insulin does: it occupied insulin receptors in the liver and muscles and ordered them to remove glucose from the bloodstream and store it as glycogen. The cinnamon not only mimicked insulin, it enhanced insulin receptor sensitivity to insulin. They showed that insulin plus MHCP provided an effect that was greater than the sum of the parts. Taken over a period of several months, MHCP helped insulin receptors to heal.

When cinnamon extract (Cinnulin®) was given to human patients who had insulin resistance, the results were dramatic. After 40 days of treatment, blood sugar levels were reduced by 18-29%. This means that an insulin resistant patient (e.g., type 2 diabetes or metabolic syndrome) with an average blood sugar level of 120 could expect reductions down into the normal range (80-90) simply by taking MHCP cinnamon.



### *Cinnamon*

Whole cinnamon is *not recommended* as it contains naturally-occurring coumarin, which has activity similar to the commonly-used blood thinning drug, Coumadin. Consuming large quantities of supermarket cinnamon on a regular basis might therefore pose a health risk, especially for individuals taking blood thinners. Coumarin is removed from quality cinnamon extract products marketed as “Cinnulin®” nutritional medicinals.

Cinnulin® cinnamon extract will also reduce blood lipids. The MHCP in it has been shown to reduce total cholesterol, LDL cholesterol, and triglycerides.

I’ve noticed plain cinnamon spice in capsules in certain chain drugstores. Steer clear of these products; there’s no reason to believe they’d work.

Dose: 125 mg per capsule; take 2 capsules twice daily. (Do *not* use unprocessed supermarket cinnamon.)

### **Alpha lipoic acid**

Alpha lipoic acid (ALA), a powerful broad-spectrum antioxidant, reverses insulin resistance and supports several other critical aspects of heart health. ALA protects the endothelium, reduces oxidative stress, and recycles other heart protective antioxidants (especially vitamins C and E).

Dose: Supplied as 100 mg tablets. Take 200-1200 mg per day.

## Glucose Control

This combination of nutritional medicines reverses insulin resistance by bolstering the body's sugar management systems:

- **Biotin** 1,250 mcg
- **Vanadium** (as vanadyl sulfate) 500 mcg
- **Chromium** 400 mcg
- N-Acetyl-L-Cysteine USP 250 mg
- **Alpha-lipoic acid** 150 mg
- **Banaba** (*Lagerstroemia spectrosa L.*) 24 mg
- **Gymnema sylvestre** leaf, dried extract, min. 25% gymnemic acid 200 mg

Dose: Renewal Research Glucose Control. 1-2 capsules twice daily;

## Chromium

Take 200-1000 mcg/day. (Or take Glucose Control.)

## Flaxseed oil

(Barlean's brand) - one tablespoon or 6 caps daily

## Address other markers for TMS

### Lowering your triglycerides lowers blood sugar

See complete triglyceride lowering program in Chapter 7.

- Restrict carbohydrates! A low carbohydrate diet is essential for lowering triglycerides. Excess carbohydrates drive triglyceride levels up. No refined carbs and no sugars. Small quantities of unprocessed complex carbohydrates are acceptable. Replace high carb foods with nuts and seeds.
- Low fat diet. Dietary fats, especially animal fats and hydrogenated oils elevate triglyceride levels.
- Garlic and onions or garlic extract capsules (2-4 twice a day).
- Acetyl-L-Carnitine (500-1000 mg twice a day).
- Policosanol (20-40 mg daily).
- Full daily recommended dose of a top quality multivitamin/mineral formula.
- Flaxseed oil (1 tablespoon or 6 capsules daily).

### Raising your HDL lowers your blood sugar

- See HDL section in Chapter 7.
- Aerobic Exercise, e.g., jogging or fast walking one hour a day.
- Low cholesterol diet; discontinue animal fats; excess animal fat consumption lowers HDL.
- Garlic, either dietary or as a daily supplement (2-4 capsules twice a day).
- Acetyl-L-Carnitine has also been shown to significantly raise HDL cholesterol.

## **Lower your blood pressure**

If your blood pressure is elevated (above 130/85), your first line of treatment should be exercise. In 85% of people with mild to moderate hypertension, exercise alone is curative. In most cases, daily exercise, a low carb diet, and weight loss will gradually lower blood pressure into the normal range without the need to resort to drugs. I've already described the kind of exercise program this requires.

If you've given it an adequate trial (one hour of aerobic exercise a day for two months) and exercise alone truly does not work, continue the exercise program, and add nattokinase (see Chapter 10 for details).

If, after two months, your blood pressure is still elevated, ask your doctor to start you on hydrochlorothiazide, a gentle diuretic that is generally well tolerated. (Many antihypertensive drugs are toxic, so avoid them unless absolutely necessary.)

Keep in mind that a diet rich in fresh fruit and vegetables will go a long way toward controlling hypertension.

## **Weight loss (getting rid of the abdominal fat)**

The abdominal fat deposits (less sensitively known as "pot belly") that characterize TMS will melt away naturally when you follow the low carb diet and daily exercise program described above.

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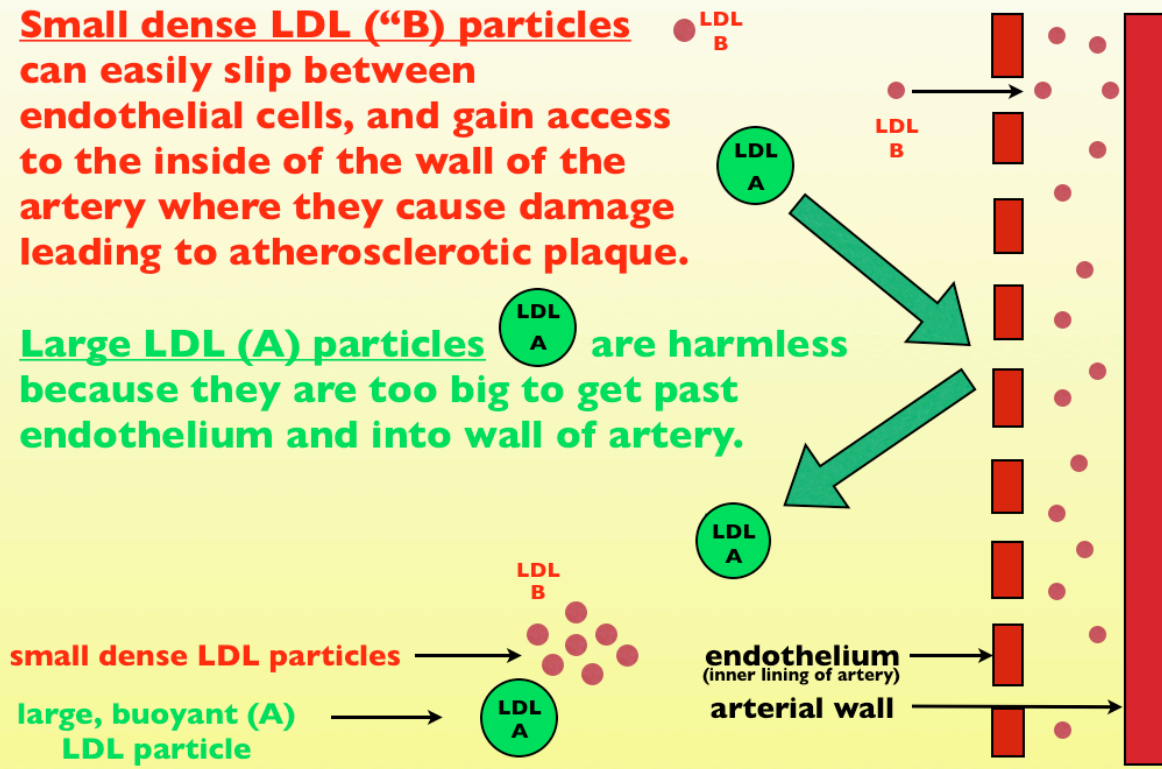
Now let's take a look at how the size of your LDL particles dramatically influences cardiovascular risk...



# LDL Particle Size

**Small dense LDL (“B) particles** can easily slip between endothelial cells, and gain access to the inside of the wall of the artery where they cause damage leading to atherosclerotic plaque.

**Large LDL (A) particles** are harmless because they are too big to get past endothelium and into wall of artery.



## *Chapter 12*

# **LDL Particle Size**

## **A Few Nanometers Can Spell the Difference Between Life and Death**

### **Bigger is better and small is not beautiful**

Most people know that excess LDL particles—too much “bad cholesterol”—can cause heart attacks. Few appreciate, however, that LDLs come in different sizes, and that LDL particle size is intimately linked to risk. Specifically, larger LDL particles are relatively benign, while smaller LDLs spell danger.

In the 1980s, researchers began questioning the predictive accuracy of cholesterol and the lipid panel. It was no secret that 75 percent of patients with myocardial infarctions had normal LDL and HDL. In the landmark Framingham Study, 80 percent of the patients with a cardiovascular “event” had lipid levels identical to the population that was event-free. At best, only about 40 percent of premature cardiovascular disease can be accounted for by factors in the lipid panel. Clearly, a more precise version of the lipid panel was necessary.

In 1988, scientists led by Dr. Ronald M. Krauss, head of the Department of Molecular Medicine at the University of California’s Lawrence Berkeley Laboratory, first established a link between smaller, denser LDL particles and the subsequent development of heart disease. Dr. Krauss’s paper says, “The LDL subclass pattern characterized by a preponderance of small, dense LDL particles was significantly associated with a threefold increased risk of myocardial infarction.”

In his presentation at the American Heart Association's 67th Scientific Sessions in Dallas, Dr. Krause said, "Since heart attacks often occur in people whose total cholesterol levels put them at only moderate risk—those with readings in the 200-240 mg/dl range—it is hard to pick out the person who's going to get heart disease. That's why it is important to look at other factors such as LDL that might aid in that prediction."

### **Can a billionth of a meter change your life?**

You bet. Turns out there’s a tight relationship between the diameter of an LDL particle and cardiovascular risk. For every nanometer (nm; one billionth of a meter) *decrease* in LDL particle size, cardiovascular risk *increases* by 200 percent. Think of it: a decrease in size of your LDL

particles of *one billionth of a meter* more than *doubles* your risk of a heart attack or stroke! Whoa.

Why is LDL size so important? How can a billionth of a meter of *anything* spell the difference between life and death? Though it may not be true in other aspects of life, down in the nanoscale world of LDL particles, bigger really *is* better. Smaller, denser LDLs can easily slip through the small space between endothelial cells and thus gain access to the inside of the arterial wall where they initiate plaque. Meanwhile, their larger, less dense fellow travelers are denied access simply because they are too big to wiggle through.

It helps to think in terms of beach balls and bullets here. Large sized LDL particles (the beach balls) ricochet harmlessly off the arterial wall, while small LDL (the bullets) penetrate the artery's endothelium and start causing trouble.

Your endothelium (that single layer of flat, skin-like cells that line the inside of your blood vessels) provides a protective wall that blocks entry of larger LDL particles into the arterial wall. A healthy endothelium does a good job of protecting the artery below from unwanted items. If the endothelium becomes inflamed, however, it is unable to stop the smaller LDLs from breaking through the barrier—and when this happens, molecular mayhem ensues, leading directly to atherosclerotic plaque, heart attacks, and strokes.

What is the actual size difference between those denied access and those allowed in? For me, this is where things get surreal. That difference would be 0.7 nanometers, slightly less than a billionth of a meter, a value so small that non-physicists may have trouble grasping it. What kind of lilliputian laws give seven-tenths of a nanometer the power to decide between life and death? If this doesn't kindle a newfound awe and respect for the colossal power and leverage of cellular and sub-cellular molecular events, I don't know what would.

## **Pattern “A” is “All Right” but Pattern “B” is “Bad”**

LDLs average about 25 to 26 nanometers (nm; billionths of a meter) in diameter. To get an idea of just how small LDL particles are, consider this: you'd have to line up ten million of them side by side to make a line just an inch long. Clinical pathologists classify LDL particles into two main groups: large (“Pattern A”) and small (Pattern “B”). The large LDLs of “Pattern A” are greater than 25.7 nm in diameter. Small, dense LDLs, those in “Pattern B,” have diameters less than 26.4 nm. (Intermediate sized LDL particles range between 25.8- 26.3 nm.)

Individuals with large LDL (“Pattern A”) particles are at significantly lower risk of atherosclerotic disease. Conversely, people with small dense (Pattern “B”) LDL particles are at greatly increased risk of atherosclerotic disease.

(I was having a hard time remembering which type was desirable and which not, so I came up with this arbitrary mnemonic device: “A” stands for “All right” and “B” stands for “Bad.” This may seem a bit hokey, but it works for me.)

## **Type “B” more easily oxidized**

There is another reason you want the large fluffy “A” type particles: Small, dense, “bad” “B” LDLs are more vulnerable to oxidation than their larger, healthier compatriots. Smaller particles have a greater surface area to mass ratio, and thus provide a bigger target for oxidizing agents. This provides yet another reason for taking daily doses of antioxidants like phytonutrients, alpha lipoic acid (100-600 mg/day), vitamin E (as mixed tocopherols, 400-2000

IU/day), vitamin C (2000-10,000 mg/day), coenzyme Q-10 (as Coenzyme QH, the reduced form, 50-300 mg/day), and carotenoids (as mixed carotenoids 10,000 IU/day). By protecting LDL from oxidation, these nutritional medicines lower the risk of heart disease.

## **Don't confuse LDL particle size with LDL number**

Don't confuse *LDL* particle number (which is part of the Lipid Panel) with *LDL particle size* (a different test, also called a "VAP"). They are two completely different markers for cardiovascular risk. LDL is a *type of particle* called LDL (HDL and VLDL would be examples of other particle types.) LDL particle size measures the *actual diameter* of your LDL particles; the lab result is actually a distribution of the various sizes of all your LDL particles.

Simply having a high LDL doesn't mean one is doomed to have more of the small bad "B" type. Conversely, a low LDL doesn't imply an "A Pattern." Studies have shown, however, that people with more of the undesirable "B" type are more likely to be males, more likely to have elevated triglycerides and elevated apolipoprotein(a), and more likely to have less HDL ("good") cholesterol) level.

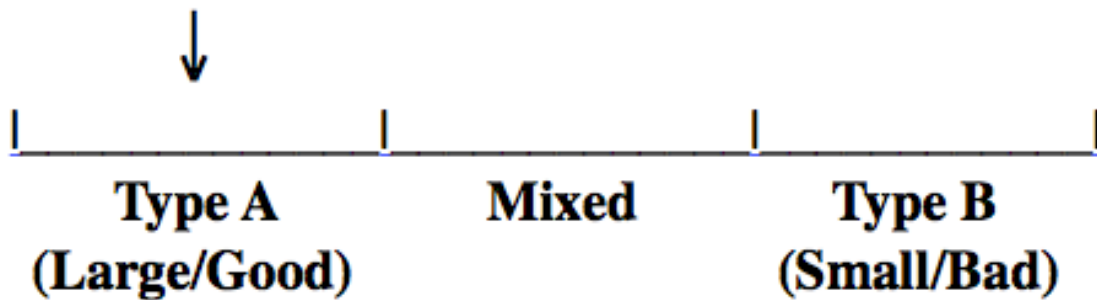
Studies also show that people with a high cholesterol *and* small dense ("B" type) LDLs appear to receive more benefit from cholesterol lowering treatment than those with a high cholesterol and large ("A" type) LDLs.

Small, dense Pattern "B" LDL particles are also more prevalent in persons with the pre-diabetic metabolic (insulin resistance) syndrome. Treating an elevated blood sugar and reversing the metabolic syndrome (see Chapter 10) will shift the pattern away from "B" and toward preferable Pattern "A."

## **Testing for LDL Particle Size**

So how can you determine whether your LDL particles are bouncing beach balls or deadly bullets? Get tested. There are three different techniques for measuring particle size. Berkeley HeartLab Inc. offers an LDL gradient gel electrophoresis. LipoScience Inc. offers a nuclear magnetic resonance (NMR) method; and Atherotec Inc. uses their vertical auto profile (VAP) test. The results for all three are comparable.

The results printout provides a bunch of confusing data about various types of particles, but all you need to do is locate the summary that tells you whether your particles are predominantly small ("Pattern B") or big ("Pattern A"). You might be somewhere in between these extremes; this is call "Mixed Type." The printout usually looks something like this:



*Note that the arrow points to where you are on the spectrum from good “A” type to bad “B” type. (In this example the patient has mostly good “A” type particles.)*

### **The triglyceride/HDL shortcut**

Triglyceride lowering treatments create large fluffy LDLs. HDL elevating treatments create large fluffy LDLs. You can use this information to save money on LDL particle size retesting. If, on initial testing, your LDL particle size turned out to be Type “B,” you can track your treatment program progress by following the (less expensive) HDL and triglyceride levels on your lipid panel. If your HDL was low and is now coming up, and if your TG was high and is now coming down, you can safely assume your program is also working to increase your LDL particle size.

# **How to Increase Your LDL Particle Size**

**(From Bad Pattern “B” to All Right Pattern “A”)**

## **How to Shift Your LDL Pattern from “Bad B” to “All right A”**

**Daily Exercise**

**Low carb diet**

**Reduce triglycerides** (see Chapter 7)

**Raise your HDL level**

**Lower your blood sugar level** (if elevated)

**Vitamin E** - 800-1200 IU daily

**Flaxseed oil** - one tablespoon or 6 caps daily

**Reduce fasting blood sugar** (if elevated)

**Weight loss**

### **Low carbohydrate diet, daily exercise, weight loss.**

Want to trade your bullets in for beach balls? By now this must seem like a broken record, but here I go again: **carbohydrate restriction, daily exercise (and the weight loss they generate)** dramatically enhance conversion of small dense LDL to bigger, softer, fluffier Type “A” LDL particles. (See Chapter 11.)

### **Lower your triglycerides**

**All triglyceride-lowering therapies (such as low carb dieting) also shift LDL particle size toward the large fluffy type “A.”**

The same diet and exercise prescriptions that successfully manage lipid abnormalities (by this I mean lower your cholesterol, LDL and triglycerides, and raise HDL) will also shift the size of LDL particles toward the beneficial large buoyant type. You already know the drill: daily exercise (at least one hour), weight loss (it’ll come naturally with daily aerobic exercise), no processed foods, mostly organic foods, no refined sugars, and dietary restriction of animal fats and carbs. Avoid fatty dairy products and fatty meats. Replace saturated fat with plant-derived monounsaturated fats, such as coconut, palm, olive, flaxseed, or walnut oil.

See Chapter 7: The Lipid Panel.

### **Raise your HDL levels (if low, which they probably are)**

The same diet and exercise prescriptions that successfully raise HDL will also shift the size of LDL particles toward the beneficial large buoyant type.

## Lower your blood sugar levels (if elevated)

If your fasting glucose is over 90, treat insulin resistance (see Chapter 11). Without fixing the blood sugar regulation problem, the LDL particle size will not revert to normal. With blood sugar control, however, LDL particle size will move in the desired direction (i.e., larger). Raising your LDL particle size provides yet another reason to give up that sedentary lifestyle, avoid the sugars and animal fats, and eat low carb.

Replace saturated fat with plant-derived monounsaturated fats, such as olive or coconut oil.

## Nutritional medicines that increase LDL Particle size

- **Vitamin E**—Prevents oxidation of LDL (see Chapter 5). Take 800-1200 IU/day (prevents oxidation of LDLs) as mixed tocopherols, 800-1200 IU/day.
- **Flaxseed oil**—Prevents oxidation of LDL particles. Take one tablespoon of liquid (or six—1000 mg capsules) daily.
- **Marine Lipids** (fish oils)
- **If blood sugar elevated**
  - **Alpha lipoic acid**—200-600 mg a day
  - **Cinnamon extract**—Cinnulin® brand specially prepared coumarin-free extract containing minimum of 3% type-A polymers; take two capsules twice daily.
  - **Glucose Control** (Renewal Research)—nutritional medicines that reverse insulin resistance and bolster the body's sugar management systems. Dose: 1-3 capsules twice daily. Contains:
    - Biotin 1,250 mcg
    - Vanadium (as vanadyl sulfate) 500 mcg
    - Chromium 400 mcg
    - N-Acetyl-L-Cysteine USP 250 mg
    - Alpha-lipoic acid 150 mg
    - Banaba (*Lagerstroemia spectrosa* L.) 24 mg
    - Gymnema sylvestre leaf, dried extract, min. 25% gymnemic acid 200 mg

## Drugs\* that increase LDL Particle size

- Tricor
- Gemfibrozil
- Niacin
- Metformin
- Actos
- Avandia

\* I don't recommend taking these; they are included for informational purposes only.

# Final Thoughts

*Of all the things I've lost, I miss my mind the most.*

*—From a bumper sticker spotted in Berkeley, California*

By now you know how strongly I feel about the importance of sidestepping the locomotive hurtling toward two out of every three of us.

Look to your left. Look to your right. Atherosclerosis will deliver an early departure to two of you.

When you consider the stakes—we're talking life or death here—those aren't very good odds. But for me personally, premature death from a heart attack is not nearly as scary as suffering a non-lethal stroke and having to live the rest of my life without a functioning brain. Let me share one final story to try to illustrate this idea.

Medical school, as I remember it, was a seemingly endless blur—a procession of days crammed full of powerful images of disease and healing, life and death. One day you'd be in surgery, holding retractors during a coronary bypass, the next might find you administering electroencephalograms (EEGs) or delivering babies. It was sort of like a marathon showing of ER reruns, except these episodes were all too real. You'd catch a little sleep, then jump right back into the maelstrom as the endless succession of intense dramas started all over again.

Of all the images that bombarded my senses during my medical school years, one remains indelibly etched in my memory. I want to share it with you because it so vividly illustrates why a healthy brain, free of atherosclerotic plaque, is indispensable for all else life has to offer.

It happened during my junior year. After two years of basic science courses, my classmates and I had finally begun our clinical training. At last, we were seeing real live patients rather than reading about them in textbooks.

My first clinical assignment was on the neurology wards. Rounds were usually held in the university hospital, but on one appropriately gloomy wintry day, we were summoned to a chronic care facility far removed from the main campus. I'm sure we looked for all the world like a flock of eager ducklings as we trundled along behind Bob Townsend, M.D., our neurology professor.

After looking in on an assortment of chronic neurological patients, Dr. Townsend stopped abruptly in front of the closed door to a private room. "Please don't talk while we're in this room. I'll explain later." Then he held open the door, and one by one, we quietly filed in.

Inside, the scene was surreal--and depressing. The room was darkened and eerily quiet. A gaunt old man in a white hospital gown lay flat in the bed, passive and motionless. His head was propped up on a pillow, and he stared, expressionless, in the general direction of a television set that was turned on but had no picture or sound--just the fuzz you get when a channel isn't tuned in.

He didn't react to our presence. No body movement, no utterance, no blink--just a sunken, glassy gaze. The darkened room, the lifeless yet living man, Dr. Townsend's secrecy--all of it gave me the willies. My classmates also suspected something unusual was up. They began shooting furtive glances back and forth, as if to say, "This is weird. What gives here?" Though the man was clearly alive, he was, in a sense, more dead than alive.



Obviously not in a mood to linger, Dr. Townsend performed one of the fastest and most perfunctory neurological exams I've ever seen. Almost as soon as we had entered the room, we found ourselves back outside in the hall.

Dr. Townsend quickly slipped into teaching mode, grilling our eager little group on comas and strokes and brain syndromes. We weren't the first group of would-be clinicians he'd seen, nor would we be the last. He rapidly moved us through a series of questions designed to help us understand what living brains do, what dead--or dying--brains cannot do, and how all this applied to the patient we had just seen.

Dr. Townsend then explained that this gentleman had totally lost his cognitive functioning as a result of cerebrovascular disease. In effect, atherosclerosis had choked off the blood supply in the arteries feeding his brain. He had been totally unresponsive for years. "Because he is unable to respond, we don't know whether he can see, hear, smell, or even think. That is why I asked you not to talk. It is possible, though rather unlikely, that he could be able to hear you.

"Only his cognitive and motor centers are affected--not the vegetative ones, which control bodily functions like heart rate and digestion," Dr. Townsend continued. "His vital signs are normal. It is possible that he could perceive or experience stimuli, like our conversation. But because he is totally unable to react to stimuli by initiating voluntary motor behavior, he has absolutely no way of responding. So we don't really know whether he is thinking and, if he is, what he's thinking about."

When we were just about to move along to the next room, Dr. Townsend--almost as an afterthought, in a tone that seemed to seek immunity for him and the rest of us from a similar, cruel fate--quietly revealed the man's identity: "Gentlemen," he said, "that was Theodore Jenkins."

What a shock. A tingly feeling went up my spine. We all knew the name, but no one had recognized him. That shell of a man was none other than the recently retired president of the university. He had been a mental giant, a man of the most impeccable intellectual credentials. His brain had served him well.

On the way home, a profound sadness came over me. I wondered how such a fate could befall such an intelligent, accomplished man. To be alive without a functioning brain seemed a horrendous fate. Why did his physical body have to live out its life span when his brain had already checked out? To see him incapacitated that way triggered a cascade of strong feelings and a myriad of questions about life and death.

Beyond these imponderables, certain facts were clear. Dr. Jenkins was a victim of our medical ignorance. He had suffered the consequences of cerebral atherosclerosis in the days before we knew that this conditions could be prevented and reversed through the kind of diet, supplementation, and exercise described in this book. Deprived of these protections, atherosclerosis had choked off the blood supply to his brain cells.

Thanks to what we've learned in the 40 or so years since this scenario played out, we now have the ability to protect the brain, heart, and entire vascular system from the ravages of atherosclerosis. The information in this book can help you protect that vital resource between your ears so you can keep your mind's fires burning as brightly as possible for as long as possible.

So—one last time—I strongly urge you to [GET TESTED!](#)

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## About the Author

Timothy J. Smith, M.D. has been studying and practicing alternative, nutritional, and conventional healing principles for over 40 years. As an undergraduate he drifted about, accumulating transcripts from the University of Wisconsin, University of Illinois, Northwestern University, and Harvard University. In his early 20s he set his sights on a career in medicine. He graduated from the University of Cincinnati College of Medicine in 1970, completed his internship at the Presbyterian Hospital, Pacific Medical Center in San Francisco and his residency at the University of California, San Francisco Medical Center. He subsequently established a general family practice in Berkeley, California, where he integrated conventional medical practice with alternative modalities and molecular medicine. Dr. Smith's current practice consists of telephone consultations with doctors and patients around the world. He specializes in difficult diagnoses and designs alternative and integrative medical treatment programs for a wide variety of medical conditions, including nutritional medicine protocols for the reversal of atherosclerotic heart and cardiovascular disease.

A longtime student and advocate of Chinese Traditional Medicine, Dr. Smith was instrumental in introducing acupuncture to the American medical community. In 1972, he founded the first publicly funded acupuncture clinic in the United States. In 1977, Dr. Smith joined the first delegation of American physicians practicing Chinese Traditional Medicine to visit the People's Republic of China. Dr. Smith is a founding member of the American Academy of Medical Acupuncture and past vice president of the American Acupuncture Association and has participated in designing the first national American Academy of Medical Acupuncture certification examination for physicians and the state licensing examinations for non-physician acupuncturists in California and Florida.

Recognizing that the same concepts that apply to healing are also effective for prevention, and with a career-long interest in deciphering the biochemical causes of illness, in the 1980s Dr.

Smith shifted his focus to clinical applications of new research developments in molecular and cell biology. His emphasis on prescribing nontoxic, plant-based medicines signals a shift in the dominant medical paradigm away from symptom-suppressing pharmaceuticals and toward natural medicines that address the underlying molecular biological causes of disease and nourish the healing process. To encourage application of these principles in everyday life, in 1999 Dr. Smith published *Renewal: The Anti-Aging Revolution* (Rodale Press; St. Martin's Press), a 680 page book presenting a program of diet, supplementation, and exercise for slowing and reversing the aging process and creating optimum health.

After publishing *Renewal*, Dr. Smith turned his attention to applying the latest research developments in molecular biology and nutritional medicine to prevent and reverse atherosclerotic cardiovascular disease (heart attack and stroke). This book represents the culmination of that work, with astonishingly successful outcomes in hundreds of patients over a span of fifteen years.

Dr. Smith is a member of numerous professional organizations, including the American Academy of Anti-Aging Medicine, the American College for the Advancement of Medicine, and the Physicians Committee for Responsible Medicine.

Dr. Smith lives in Sebastopol, California, with his wife, Dellie, and their two daughters.

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## **Chapter 8—C-Reactive Protein: The Fire Alarm Molecule**

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## **Chapter 9—Homocysteine: Sandblaster From Hell**

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## **Chapter 10—Fibrinogen: Clotting factor and inflammatory protein**

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## **Chapter 11—Blood Sugar, Insulin Resistance, and The Metabolic Syndrome**

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## Chapter 12—LDL Particle Size

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